Board of Health
Agenda

Date: July 12, 2023
Time: 2:00 PM
Location: Conducted by Remote Participation

1. Administrative

   BOARD OF HEALTH MEETING AGENDA

   Date: Wednesday, July 12, 2023
   Time: 2:00pm
   Location: Conducted by Remote Participation

   In accordance with the Governor's Order Suspending Certain Provisions of the Open Meeting Law, G. L. c. 30A, § 20, the July 12, 2023 public meeting of the Arlington Board of Health shall be physically closed to the public. The meeting shall instead be held virtually using Zoom.

   Zoom Login instructions:
   Instructions and the meeting link for this specific meeting can be found on the Board's agenda and minutes page or on the Town's meeting calendar. The meeting registration information is listed below. When attendees enter the meeting, they will be placed into a virtual waiting room. Attendees will be admitted into the meeting from the waiting room at the start of the meeting.

   Please register in advance for this meeting: https://town-arlington-ma-us.zoom.us/meeting/register/tZMvf-qoqzovE9Iqaro2Vbt7F_WcSM9eSju3#/registration

   On this agenda:

2. Acceptance of Meeting Minutes from June 7, 2023
3. HEARING:
   Abcellera Boston - Large Scale
4. HEARING:
   Tobacco Violation - Fenway Market
5. UPDATES:
   Environmental Health
6. UPDATES:
   Restaurants
7. UPDATES:
   Public Health Nurse

PUBLIC COMMENT

Adjourn

Town of Arlington
Department of Health and Human Services
Office of the Board of Health
27 Maple Street
Arlington, MA 02476

Tel: (781) 316-3170
Fax: (781) 316-3175

BOARD OF HEALTH MEETING MINUTES

Date: Wednesday, June 7, 2023
Time: 2:00pm
Location: Conducted by Remote Participation

In accordance with the Governor's Order Suspending Certain Provisions of the Open Meeting Law, G. L. c. 30A, § 20, the June 7, 2023 public meeting of the Arlington Board of Health shall be physically closed to the public. The meeting shall instead be held virtually using Zoom.

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Please register in advance for this meeting: **https://town-arlington-ma-us.zoom.us/meeting/register/tZwpdO-hrzovGdBM-tvRgnfhlZYN6k_Sw7NI#/registration**

On this agenda:

Public Health Director, Natasha Waden, made the following statement. Consistent with the Governor's orders suspending certain provisions of the Open Meeting Law, this Town of Arlington Board of Health meeting is being held virtually via Zoom for audio and video participation of Board Members and the public. When you entered this meeting, you were automatically muted. During this meeting you will be unmuted individually as needed. These controls are in place to ensure that today's meeting is safe and effective. At this time, I would like to confirm that all members and persons anticipated on today's agenda are present and can hear me.

Board Members, when I call your name and unmute you, please respond in the affirmative.

1. Dr. Marie Walsh Condon, Aye Present
2. Dr. Laura White, Aye Present
3. Dr. Peter Rice, Aye Present

Health Department staff, please respond in the affirmative when I call your name and unmute you.

1. Laura Munsey, Aye Present

DRAFT

2. Jessica Kerr, Aye Present
3. Pat Martin, Aye Present
4. Cameron Bishop, Aye Present

Applicants and Representatives, do we have anyone on the call representing an application?

1. Body Art Variance Request - Lily Jarnryd, Aye Present
2. Body Art Practitioner Application - Jonathan Santos representing Zachary Young, Aye Present

Thank you everyone.

As stated, this Open Meeting of the Arlington Board of Health is being conducted remotely consistent with the supplemental budget bill signed by Governor Healey on March 29, 2023.

The Order allows public bodies to meet entirely remotely so long as reasonable public access is afforded so that the public can follow along with the deliberations of the meeting.

Ensuring public access does not ensure public participation unless such participation is required by law. This meeting will have several public comment periods, one during each of the hearings and one at the end of the meeting. If you would like to comment during one of the public comment periods, please use the "Raise Hand" function if on a computer, or "Dial *9" if on the phone. When your name or phone number is called, and you are unmuted, please state your name and provide your comment. All attendees will be afforded 3 minutes for any comments.

For this meeting, the Board of Health is convening by telephone and computer conference via Zoom as posted on the Town's Website identifying how the public may join.

Only Health Department staff will be able to share their screen during this meeting. Board Members and Department Staff may be participating by video conference. Accordingly, please be aware that other folks may be able to see you. Anything that you broadcast may be captured by the recording.

All of the materials for this meeting are available on the Novus Agenda dashboard, and I recommend that Board Members and the public follow the agenda as posted on Novus unless otherwise noted. Members of the public are encouraged to provide written public comments.

Before we get to today's agenda, I am going to cover some ground rules for effective and clear conduct of our business and to ensure accurate meeting minutes.

Marie Walsh Condon, the Board Chair, will introduce each agenda item. After the item is presented, she will go down the list of Board Members, inviting each by name to provide any

comment, questions, or motions. Please hold comments or questions until your name is called and you are unmuted.

For any response, please wait until the Chair yields the floor to you, and state your name before speaking.

Finally, each vote taken during this meeting will be conducted by roll-call vote.

Floor yielded to Dr. Marie Marie Walsh Condon who reviewed today's agenda.

Agenda Items

1. Acceptance of Meeting Minutes from May 24, 2023

   Motion made by Dr. Laura White to approve the May 24, 2023 meeting minutes as submitted.

   2nd by Dr. Peter Rice.

   Vote:
   - Dr. Marie Walsh Condon, Aye
   - Dr. Laura White, Aye
   - Dr. Peter Rice, Aye

   Approved (3-0) Unanimous

2. HEARING:
   Body Art Variance Request - Lily Jarnryd

   Inspector Bishop reviewed variance request for Lily Jarnryd to work at Benchmark Tattoo. He reported that Benchmark Tattoo has a very extensive training program including cleaning procedures, bodily fluid safety, disease prevention, etc. but noted that Lily is looking for a variance because she does not have the required training to become a practitioner.

   Floor yielded to Lily Jarnryd who reported she reported she has always has been an artist, and likes to help people express themselves through art and believes this job is perfect for her.

   Dr. Walsh Condon reviewed Lily's application and noted that she has received blood born certification and is working towards her license.

Dr. Laura White has no questions or comments.

Dr. Peter Rice finds this application and process very interesting, and had questions for the professional staff. Dr. Rice stated this is a profession that requires specializes skills and expertise and in our Regulations we require two years of actual experience, yet there is no standards at the local or state level, and inquired where the standards come from.

Director Waden stated there are model regulations from Massachusetts Association of Health Boards (MAHB), and the Massachusetts Health Officers Association (MHOA) who advise communities regarding such matters. The Arlington Health Department has also reviewed other regulations from communities such as Boston, Cambridge, and Somerville, and we are all basing our local regulations off of the model regulations, and National Model Regulations are provided by the Massachusetts Environmental Health Association (MEHA). The existing Regulation is one that we have had for some time, and at some point in the future, we will explore and update some changes that can be accommodated. Director Waden also stated when the next regulation review comes up, we will look at other communities and review their regulations, and look at both the state and national levels, and will present to the Board what those best practices are, and solicit feedback from the Board and Practitioners as well. The Board of Health does have the authority to make regulations that would be protective of the community and this falls under that purview.

Dr. Peter Rice stated he does understand the public health issues regarding infection and the Board of Health's role, but was interested in some of the certifications required. Director Waden stated that when we update our Regulations we will want to look at the new trends, and current requirements, and the existing regulations were adopted many years ago, and some of those requirements may have changed and will be reflected in updated regulations.

Dr. Walsh Condon said close to 25 years ago we first developed this set of Regulations. She further noted that the next calendar year these Regulations are slated to be reviewed and updated, and believes some parts of the existing requirements may be extraneous or outdated at this point.

Jonathan Santos from Benchmark Tattoo stated he has been licensed in many communities in Massachusetts as well as in other states and commented that the bar is typically set pretty high in this profession with the requirements needed compared to other careers that may even have more liability. He also commented that the extraneous fees compared to other businesses are also a big difference.

Motion made by Dr. Walsh Condon to approve the Body Art Apprentice Variance Request for Lily Jarnryd as written.

2nd by Dr. Laura White

Vote:
- Dr. Marie Walsh Condon, Aye
- Dr. Laura White, Aye
- Dr. Peter Rice, Aye

Approved (3-0) Unanimous

3. HEARING:
Body Art Practitioner Application - Zachary Young

Inspector Bishop stated he reviewed Zachary Young's Application to become a Body Art Practitioner at Benchmark Tattoos, and stated Zachary is currently licensed in Gainesville Florida and he has demonstrated over numerous years that he has the capabilities and professionalism to be a Practitioner of Body Art. Inspector Bishop further stated Zachary has shown his dedication and knowledge through his blood pathogen training, CPR training, as well as other documentation he provided with his application.

Jonathan Santos of Benchmark Tattoo stated he worked with Zach for a few years in Florida, and had the privilege to watch him come through his apprenticeship. He stated Zach has over 5 years of experience, is one of the more qualified tattoo artists to walk through the door. He reported Zach is in the process of relocating to this area.

Dr. Laura White inquired if Hepatitis B testing or Vaccination is required in our Regulations. Inspector Bishop stated the current Regulations do require disclosure of vaccination status.

Dr. Marie Walsh Condon further stated the Regulations require disclosure of vaccination status, not a requirement of vaccination. The requirement is to show vaccination status. The public health reason for this is in case there is a question of transmission, there is a paper trail available.

Dr. Peter Rice had no additional questions or comments.

No public comments

Inspector Bishop recommends approval of this Application.

Motion Made by Dr. Marie Walsh Condon to accept the Body Art Practitioner Application of Zachary Young as submitted.

2nd by Dr. Laura White

Vote:
- Dr. Marie Walsh Condon, Aye
- Dr. Laura White, Aye
- Dr. Peter Rice, Aye

Approved (3-0) Unanimous

4. UPDATES:
   Environmental Health

   Director Waden shared the Arlington Health Department is part of a public health excellence collaborative and in the past couple of years we have been working with Somerville, and we have officially switched over to a new collaborative including Brookline, Belmont, and Newton. This new group met last week and we have had great communication and regional discussions for public health programs. It is also a chance to streamline the communication amongst the communities.

   The money for this grant is being utilized for a lot of staffing, and currently this collaborative has an Epidemiologist, a shared Services Coordinator, and are looking to get a Public Health Inspector, as well as additional positions in FY24. The money is in upwards of $500,000 and should provide a boost to what we will need in our community and all these communities.

   Inspector Waden reported we are all dealing with the same public health issues, and it would beneficial if we were all working from the same uniformed front and uniformed language.

   Director Waden inquired if the Board wanted to keep the July 12th meeting on the calendar, or would the Board like to cancel the meeting. After discussion it was decided to cancel the July 12th meeting, unless an emergency meeting is needed. Meetings in the Fall may need a slight time adjustment due to scheduling.

   Next scheduled meeting will be September 13th.

5. UPDATES:
   Restaurants

   Director Waden informed the Board that we were called out to an emergency oil leak at an establishment on Friday night, but we were able to respond.

Director Waden further informed the Board that Inspector Annette Curbow has left our team, but we have hired a new intern who will start on the 26th of this month.

6. UPDATES:
   Public Health Nurse

   No updates to report.

PUBLIC COMMENT

None

Motion made by Dr. Marie Walsh Condon to adjourn.

2nd by Dr. Laura White

Vote:
- Dr. Marie Walsh Condon, Aye
- Dr. Laura White, Aye
- Dr. Peter Rice, Aye

Approved (3-0) Unanimous

Thank you everyone for attending and participating in today's meeting. Have a nice day.

Meeting adjourned at 2:30 pm.

Town of Arlington
Department of Health and Human Services
Office of the Board of Health
27 Maple Street
Arlington, MA 02476

Tel: (781) 316-3170
Fax: (781) 316-3175

MEMO

To: Board of Health Members
From: Padraig Martin, Health Compliance Officer
Date: July 6, 2023
RE: AbCellera Boston

AbCellera Boston, Inc. (formerly Tetragenetics, Inc.) is a licensed biotechnology company that has been operating in Arlington, MA since 2015. There have been no known incidents during their time of operation in Arlington. They currently operate a Biosafety Level 1 (BSL-1) and Biosafety Level 2 (BSL-2) laboratory.

On April 12, 2023, the Health Department received a written proposal from AbCellera, requesting to add a room for large-scale production to their existing laboratory located at 91 Mystic Street, Arlington, MA. The Arlington Board of Health Biosafety and Recombinant DNA Regulations define 'large-scale' as the use of more than ten liters of rDNA and/or Biological Agent culture. This threshold is based on the cumulative volume of culture in all vessels throughout the institution's facility, not just a single vessel or experiment. Natasha Waden, Director of Public Health, and Padraig Martin, Lead Health Compliance Officer, reviewed the initial proposal and requested additional documentation to support their request.

The Arlington Health Department has enlisted the services of Rebecca Caruso, Biosafety Consultant, to review the proposal and supporting materials, as well as to conduct a comprehensive inspection of the facility. Mrs. Caruso has an extensive background in biosafety and is currently the Director of the Committee on Microbiological Safety at Harvard Medical School. The proposal, along with all supporting material, has been provided to Mrs. Caruso, who will present her findings at the July 12, 2023, Board of Health Meeting.

This packet includes AbCellera's proposal and supporting materials. Additionally, a copy of the Arlington Board of Health Biosafety and Recombinant DNA Regulations is provided.

91 Mystic St.
Arlington, MA
USA, 02474
T 1.617.500.7471
abcellera.com

April 12, 2023

Attention: Town of Arlington

RE: AbCellera-Boston proposal for installation of WAVE 25 bioreactor culture production system

Background. AbCellera Boston, Inc. (formerly, TetraGenetics, Inc.) ("AbCellera-Boston") occupies approximately 9,000 square feet of office and lab space at 91 Mystic St., Arlington, MA 02474. It is one of a number of global sites of AbCellera Biologics Inc., a Vancouver, British Columbia-based technology company that discovers and develops therapeutic antibodies. AbCellera-Boston's technology is focused on production of recombinant human proteins for therapeutic drug discovery using a fresh-water non-pathogenic organism *Tetrahymena thermophila*. AbCellera-Boston plans to expand its small scale *Tetrahymena* culture production (currently approved at <9.9 liter cultures), and is proposing implementation of two ReadyToProcess WAVE 25 culture devices provided by Cytiva.

Proposed Equipment. AbCellera-Boston is proposing to install two ReadyToProcess rocking WAVE™ 25 bioreactor systems that handle working volumes up to 25 liters at a time.

- The single-use cell culture bags (Cellbag™) are manufactured from multi-layer, laminated, clear USP Class VI plastics: Bioclear™ 10 or Bioclear 11. Each disposable culture bag holding 5 – 25 liters of cell culture will be secured on a rocking platform, and they will be equipped with the temperature and oxygen sensors, safety attachments and tubing for liquid collection. As part of Cytiva ReadyToProcess technology, Cellbags do not require sterilization or cleaning steps. They provide a suitable environment for cell growth, while minimizing the risk of cross-contamination.

- 2 oxygen cylinders (size 200) and 2 compressed air cylinders (size 200) will be ordered every 2-3 weeks from Middlesex Gases & Technologies and connected to the WAVE 25 systems.

- Laboratory furniture will be capable of supporting anticipated loads and uses. The bench will be clean, level, flat and sufficiently stable to withstand vibration from the rocking. Spaces between benches, cabinets and equipment will be accessible for cleaning. Bench tops will be impervious to water.

- There will be an easily accessible grounded power outlet close to the installation site of the system units.

- Below is the description of each WAVE 25 system component.

	Weight, kg	Dimensions, W x D x H, mm	Function
ReadyToProcess WAVE 25 rocker unit	32	685 x 540 x 390	Rocking platform
Tray 50	13.0	940 x 815 x 150	To accommodate 50L cell bags for growing 5 to 25 L cultures
Tray 20	11.0	880 x 685 x 150	To accommodate 20L cell bags growing 1 to 10L cultures
Lid 50	7.0	930 x 740 x 350	A lid to use with Tray 50
Lid 20	6.0	930 x 740 x 350	A lid to use with Tray 20
ReadyToProcess CBCU (Cell Bag Control Unit) Full	7.0	330 x 380 x 195	Gas mixer that delivers gas of a defined composition to the culture for online control of pH and DO (dissolved oxygen).
ReadyToProcess Pump 25	5.0	370 x 345 x 160	To accurately deliver liquid to the culture
Single-use cell culture bags (Cellbag™), 10L and 25L	5 – 25 depending on culture volume	10L culture bag fits Tray 20, 25L culture bag fits Tray 50	For culture containment

WAVE 25 System Operation. The WAVE 25 systems will be installed and tested on-site by Cytiva technical specialists. Training will be provided by Cytiva. The operation of the systems will be conducted by 2 AbCellera-Boston Laboratory Technicians and 1 Associate Research Scientist and supervised by 2 Research Scientists.

Justification for Large Culture Production. Implementation of two WAVE 25 systems is estimated to increase current biomass production capacity from multiple 1L cultures to single 25 – 50L cultures. Additionally, increased capabilities associated with the WAVE 25 system that include dissolved oxygen control will further increase volumetric production of recombinant proteins. The use of single-use culture bags will further minimize the need for glassware washing and autoclaving and consolidate production waste collection and disposal at a single location in the lab.

Security and Engineered Safety Measures. The WAVE 25 systems will be secured in a lab area with restricted access. Containment trays with capacity larger than the maximum culture volume will be placed underneath the bioreactors to contain potential spillage. Additionally, the floor area underneath the WAVE 25 systems will be waterproof, and will be surrounded by flood barriers, such

as rubber dams and absorbent socks. The use of personal protective equipment will be required to operate the systems. Culture media will be stored in closed containers (1L glass bottles) until ready to use.

Biohazardous and Chemical Hazardous Waste Disposal. Waste generated in the bioreactors will be handled according to existing protocols. *Tetrahymena* culture grown at AbCellera-Boston and spent culture media will be treated with 10% sodium hypochlorite (bleach) solution for 30 minutes before being disposed of in the sink. *Tetrahymena* culture and spent media that contain cadmium chloride (2 microgram/milliliter, EPA HW D006) will be treated with 10% bleach and collected as liquid cadmium waste in 55-gallon drums located in a designated waste room. Liquid cadmium waste ***is never*** disposed of in the sink. Solid waste (for example, single-use 25L culture bags) will be collected in solid cadmium waste. Veolia has been contracted by AbCellera-Boston to dispose of the liquid and solid cadmium waste stored in a designated waste room.

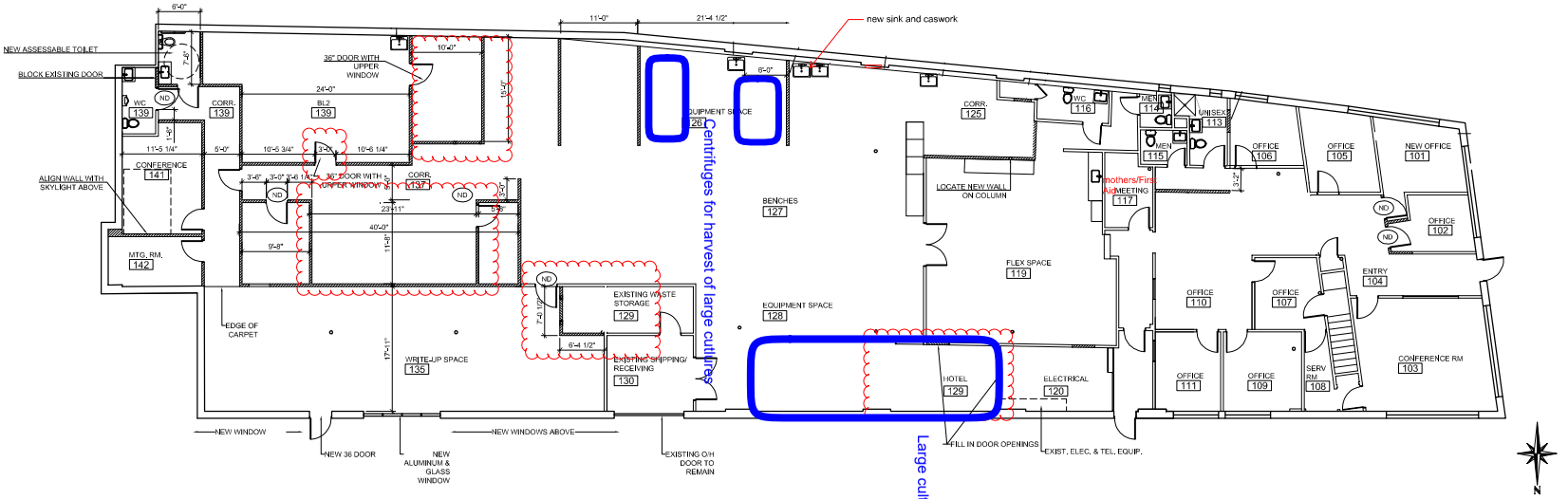
Environmental Impact Considerations. Cadmium chloride concentrations of 2 microgram/milliliter complies with the regulatory requirements of less than 1 milligram per milliliter. Single-use culture bags do not require washing after use. The increased volumes of liquid and solid cadmium waste will be handled by Veolia.

Please do not hesitate to contact me if you require further information or have questions related to this proposal.

Best regards,

Paul Colussi, PhD
Site Head & VP, Complex Membrane Protein Technologies
AbCellera Boston, Inc.

paul.colussi@abcellera.com



2 PLAN | RENOVATION
Scale: 1/8" = 1'-0"

1 PLAN | DEMOLITION
Scale: 1/8" = 1'-0"

Seal:

No	Date	Revision/Issue
*	FEB.02.23	ISSUED FOR FINAL
*	JAN.12.23	ISSUED FOR FINAL
*	NOV.23.22	ISSUED FOR REVIEW

Key Plan:

PROJECT NAME
ABCELLERA BOSTON

91 MYSTIC STREET
ARLINGTON, MASSACHUSETTS

PROJECT No:	22-117	DATE:	NOV.08.22
CLIENT No:			
DRAWN BY:	TWS	CHECKED BY:	TWS
SCALE:	AS NOTED		

DRAWING NUMBER: A2.0

Rev. No.:

TITLE: PLANS

Biological Risk Assessment Form

Study Director: complete this entire section and return to the Biosafety Officer for review

- Project name and number: Growth and induction of Tetrahymena thermophila in WAVE25 bioreactors
- Proposed agent (i.e., microorganism), biological materials, biologic or toxin of biological origin to be used: Tetrahymena thermophila, *(cadmium chloride use for the induction of gene expression is addressed in a separate job safety analysis (JSA))*
- Sponsor/Manufacturer/Vendor: N/A
- Part number: N/A
- Unit of issue (e.g., pint, liter, gallon, ml, etc.): Liter
- Maximum quantity to be stored on-site: 200L
- Quantity used per task: 25L
- How long will the task take: 48 hours per run
- Risk Group of biological agent (i.e., microorganism); check www.absa.org
  1 ☒ 2 ☐ 3 ☐ 4 ☐
    - (Inactivated Risk Group 2 agents can be generally used with BSL-1 practices and precautions)
- Has the agent (i.e., microorganism) been modified in any way? Yes ☒ No ☐
    - If so, does it make the agent more resistant to disinfection or broaden the range of cells it can enter? No
    - If the agent is attenuated and will be used with BSL-2 practices and precautions, what testing will be done to verify the attenuation(s)? N/A
    - If the agent has been modified, is the wildtype agent also available? Yes ☒ No ☐
        - If so, are special practices needed to minimize the chances of complementation? Yes ☒ No ☐
            - Please list the practices (e.g., waste segregation): Waste segregation and bleaching
- Can a less hazardous agent (i.e., microorganism) be substituted for the project?
  Yes ☐ No ☒
    - If not, can a less hazardous agent be used to do a “dry” run? Yes ☐ No ☒

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- Is this an agent (i.e., microorganism) known to be more hazardous to pregnant individuals, those with a compromised immune system or using medication to lower stomach acidity? Yes ☐ No ☒

- Is this agent listed as a CDC Select Agent or Toxin which requires a permit? Yes ☐ No ☒

    - If using an exempt amount of toxin, is a system in place to document the amount of toxin available, the amount used and the amount inactivated? Note that the system must be resistant to tampering. Yes ☐ No ☐ N/A

- If using lentiviral vectors: Not applicable ☒

    - Is a tumor suppressor further suppressed or an oncogene overexpressed? Yes ☐ No ☐ N/A

        - Please describe: N/A

    - What is the vector generation? N/A

    - Is the virus purchased ready to use or is it generated onsite? N/A

- List all employees using the proposed biological material(s): Alina Rivera, Anna Kimeu, Casey Fraher, Josefina Hernandez, Janna Bednenko, Patrick Yiang

- Describe procedure: Tetrahymena cells are cultured in a single-use Cellbag™ bioreactor container made of Fortem™ film (300 um thick film composed of 10 layers to provide strong abrasion and puncture resistance) with 25 L of rich media (peptone, yeast extract and glucose) plus 100 ug/mL of selective antibiotic Paromomycin. Cadmium chloride (2 mg/L) is added for induction of gene expression. A mix of air and pure O_2 is pumped inside the bag for aeration, with 0.5-0.25 L/ min gas flow. The Cellbag is maintained on a Wave 25 rocking platform warmed at 30-26°C for 48 hours until collection. The contents is pumped out manually into 1000 mL centrifuge flasks using a connection hose which is included in the Cellbag. Cell pellets are collected by centrifugation on Lynx 6000 centrifuges and supernatants are bleach-treated and collected in a 200 L container. This material is then collected by Veolia Environmental Services, a waste management company.

- For Risk Group 2 or above, is there a splash potential? Yes ☐ No ☐ N/A

- For Risk Group 2 or above, does the procedure generate aerosols or large concentrations (e.g., cell culture, centrifugation, sonication, homogenization, vortexing, etc.)? Yes ☐ No ☐ N/A

Biosafety Officer: complete this section

- What are the likely routes of exposure/entry?

    Absorption (open wound or mucous membranes) ☒ Ingestion ☐

    Percutaneous injury ☒ (from serological pipettes, syringes) Inhalation ☐

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- What is the infectious dose of the organism? The organism is not considered to be a human pathogen
- What is the viability of the organism in the laboratory environment?

  <2hrs ☐ >24hrs ☐ Other is known: 72-80 h
- What is the appropriate disinfectant for the biological agent or inactivation method if a toxin of biological origin? Bleaching (10% bleach)
- Is a vaccine available for this biological agent? Yes ☐ No ☒
- Has vaccine been offered to all those who will be working with agent?

  Yes ☐ No ☐ Not Applicable ☒
  - Have all declining employees submitted a signed declination to the Biosafety Officer?

    Yes ☐ No ☐ Not Applicable ☒
- What engineering controls will be used to minimize exposure (check all that apply)?

  Biosafety cabinet (BSC) ☐ Safety bucket cover or sealed rotors ☒

  Shielding ☒ Others: Click here to enter text.
- Do all employees slated to use this material have the necessary training? Yes ☒ No ☐
- Would agent specific training be useful in minimizing lab acquired infections or emphasizing special precautions to be observed? Yes ☐ No ☐ N/A
- Perform work using the following Biosafety Level:

  BSL-1 ☒ BSL-2 ☐ BSL-2 Enhanced (BSL-2+) ☐

  BSL-3 (cannot be handled at AbCellera Boston) ☐
- Work will be performed in the following lab(s) at AbCellera Boston: BSL-1 room

The Institutional Biosafety Committee (IBC) / Safety Committee (SC) has completed the risk assessment and PPE assessment below

Take the following precautions:

☐ Use in a Biosafety cabinet (BSC) ☐ Use in a glove box

☒ Special storage is required Bleached waste container (with 2 mg/L calcium chloride) is stored in a designated waste room

☒ Special warning signs must be posted: Hazardous waste labels and signage due to cadmium chloride

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☒ Wear the appropriate PPE as designated below:

☒ Safety Glasses/Splash Goggles ☐ Face Shield

☒ Lab Coat: Click here to enter text. ☐ Tyvek® sleeves

☒ Gloves ☐ Other: N/A

Comments: A spill tray will be used as secondary containment under the WAVE25 rocking platform. Appendix K of the NIH Guidelines which specifies physical containment requirements for large-scale (greater than 10 liters of culture) will be adhered to. In addition, the recommendations in Appendix M of the Biosafety in Microbiological and Biomedical Laboratories (BMBL) on large scale biosafety considerations will also be followed.

Name of Biosafety Officer: Joanna Proctor Signature:

Date: _____

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SAFETY PARTNERS
Hands-on Workplace Safety

Biosafety Practices and Bloodborne Pathogens Training January 2023

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TRAINING WILL COVER...

- What is Biosafety
- Working in the Lab
- Exposure Protection
- Biowaste and Disinfection
- Biohazard Emergencies
- Bloodborne Pathogens

What is Biosafety?

BIOSAFETY IS….

- The practices, procedures, and use of controls required to ensure safe conditions in facilities that work with potentially infectious microorganisms and other biological hazards
- In short-it is how to protect yourself, your co-workers and the environment from biohazards

BIOHAZARDS

- Human blood and blood products
- OPIM (Other Potentially Infectious Materials)
  - Human tissue or organs, human bodily fluids
  - Culture medium containing HIV, HBV, HCV
  - Human cells
- Fungal, bacterial or viral agents
- Tissue or blood from animals
- Supernatant from cells
- Effluent from living organisms

RISK GROUPS

- Biohazards are placed into risk group categories
- Specific definitions vary by organization, but all are very similar
  - CDC/NIH Guidelines-BMBL
  - Canadian Laboratory Safety Guidelines
  - World Health Organization (WHO)
  - NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules
  - European Economic Community
  - Australian/New Zealand Standard

RISK GROUPS (RG)

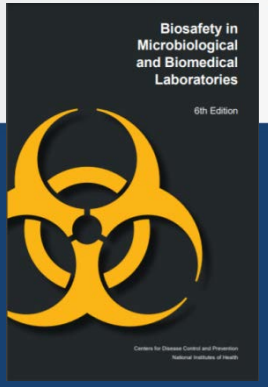
(NIH GUIDELINES, 2019)

- RG1: agents are not associated with disease in immunocompetent adult humans
- RG2: agents are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available
- RG3: agents are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available
- RG4: agents are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available

RISK GROUP DETERMINATION

- Includes review of-
  - Infectious dose of the organism
  - Virulence
  - Likely route of exposure
  - Viability of the organisms in the lab environment
  - Host range
  - Availability of suitable disinfectants
  - Availability of suitable prophylaxis

BIOSAFETY RESOURCES



- Pathogen Safety Data Sheets
  - Public Health Agency of Canada
- CDC-NIH “Biosafety in Microbiological and Biomedical Laboratories” (BMBL) 6th edition
- WHO (World Health Organization) Biosafety Manual
- Risk Group Classification for Infectious Agents
  - ABSA.org
- NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

NIH GUIDELINES/ARLINGTON RDNA TECHNOLOGY ORDINANCE

- All work involving recombinant or synthetic nucleic acid molecules must be approved by AbCellera Boston's Institutional Biosafety Committee (IBC)
  - Project registration document must be completed for each project and approved before initiation of work
- IBC meetings are generally held on an annual basis
  - Interim meetings held to approve additional project registrations and major changes to existing project registrations

ARLINGTON RDNA TECHNOLOGY ORDINANCE

- Establishes strict oversight of laboratories that engage in recombinant DNA research
- Requirements in the city ordinance are based on the NIH Guidelines
- Enforcement is carried out by the Arlington Board of Health
- An Institutional Biosafety Committee (IBC) must be formed that includes two community representatives (at least one Arlington resident)

ARLINGTON RDNA PERMIT REQUIREMENTS

- Initial notarized application from CEO; annual renewals
- Initial presentation to the Arlington Board of Health and for permit amendments
- Biosafety Manual, Chemical Hygiene Plan, Emergency Action Plan
- Pest control contract and plumbing backflow prevention
- Contract with waste management vendor such as Veolia
- Occupational health arrangement
- Formation of an Institutional Biosafety Committee

Working in the Lab

BIOSAFETY CONTAINMENT LEVELS (BSL)

- Combination of engineering controls, PPE (Personal Protective Equipment) and work practices for handling biological materials
  - Biosafety Level 1
    - Examples: Animal tissues, animal cell lines, *E. coli* K12
  - Biosafety Level 2
    - Examples: Human source materials and cell lines, HBV
  - Biosafety Level 3
    - Example: *Mycobacterium tuberculosis* (TB)
  - Biosafety Level 4
    - Example: Ebola
- Protect the worker and the public
- Risk Group (RG) and Containment Level are often the same, but not always

BIOSAFETY LEVEL

- It is common for people to assume that Risk Group (RG) and Biosafety Level (BSL) are synonymous
- An agent can be classified as RG1, but BSL-2 work practices are recommended due to
  - Generation of aerosols
  - Scale of work
  - Individual susceptibility to disease
- BSL-2 Enhanced / BSL-2+ work practices may be recommended for RG2 agents known to be infectious
- A thorough risk assessment determines the appropriate biosafety level

RISK ASSESSMENT

- A risk assessment determines the appropriate biosafety level by
  - Identifying the hazardous characteristics of biologics
  - Identifying work practices that have the potential to create exposure hazards
  - Addressing the consequences of exposure
    - » Can exposure cause a laboratory acquired infection
    - » Severity of the consequences of infection
- Recommends appropriate work practices, equipment, and facility safeguards to handle biological material
  - Identifies and addresses potential deficiencies in lab work practices

RISK ASSESSMENT FACTORS

- Includes review of-
  - Infectious dose of the organism *
  - Virulence *
  - Likely route of exposure *
  - Viability of the organisms in the lab environment *
  - Host range *
  - Availability of suitable disinfectants *
  - Availability of suitable prophylaxis *
  - Scope and scale of work
  - Personnel in the lab

**Factors also determine Risk Group (RG)*

WORKING AT BSL-1

- Standard Microbiological Practices:
  - Restrict or limit access when working
  - Prohibit eating, drinking and smoking
  - No mouth pipetting
  - Minimize splashes and aerosols
  - Decontaminate work surfaces daily
  - Disinfect waste prior to sink disposal
  - Maintain insect & rodent control program
  - PPE: safety glasses and lab coats are required when working with biological material, gloves when handling lab materials
  - Animals and plants not associated with the work being performed are not permitted in the laboratory

RG1 AGENTS AT ABCELLERA BOSTON HANDLED AT BSL-1

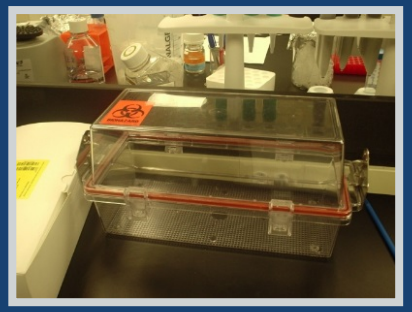
- Recombinant *Tetrahymena* cultures
- Bacterial cultures (*E. coli* K-12)
- Plasmid expression systems
- Non-toxic genes of interest

WORKING AT BSL-2

- In addition to BSL-1 practices, BSL-2 includes:
  - Lab doors must be signed and closed
  - Only authorized individuals with training may enter
  - Lab coats and safety glasses are required, gloves required when working
  - All materials must be labeled and include the biohazard symbol
    - » Source materials, waste, equipment, solutions, media

BSL-2 WORK PRACTICES

- Most work is done in a biosafety cabinet (BSC)
  - Faceshields or bench shields can be used as appropriate
- Secondary containers required for transport
- Sharps are discouraged
- Sharps waste is placed in puncture resistant containers
- Centrifuge safety cups/caps must be used
- Decontaminate work surfaces daily
- Disinfect all liquid waste in accordance with established procedures



CENTRIFUGING AT BSL-2

- All containers must be covered
- Decontaminate after use, especially if visible contamination
- Open container in a BSC or let sit for 10 minutes before opening

RG2 AGENTS AT ABCELLERA BOSTON HANDLED AT BSL-2

- Human cell lines*
- Human primary cells*
  - Human peripheral blood mononuclear cells (PBMCs)

*Potential bloodborne pathogen exposure

NOTE ON PPE

- Lab coats
  - Change regularly, place in hamper
    - » Use vendor provided bag if lab coat is potentially contaminated with biological material
  - No lab coats outside the labs
- Disposable gloves
  - Replace when contaminated, torn, punctured, or when their ability to function as a barrier is compromised
    - » Do not wash or reuse
  - Remove contaminated gloves by turning them inside out
  - No lab gloves outside the labs

SIGNS AND LABELS

- The biohazard symbol is reserved for indicating material with potential infection risks
- All human samples are considered potentially infectious
- Refrigerators, incubators, water baths and freezers containing or contaminated with biohazardous materials, and waste require a biohazard symbol
- Door signs at BSL-2 should include the agent(s) in use, precautions for entry, emergency contacts and biohazard symbol

GENERAL PRACTICES

- Wash hands frequently
  - No petroleum-based hand creams
- Disinfect equipment and bench surfaces daily
- Avoid hand contact with your mouth, eyes, nose
- Protect wounds / dermatitis
- Be prepared for an emergency
- No mouth pipetting
- No eating, drinking, or applying cosmetics in the lab
  - Includes chap stick and throat lozenges

AEROSOL CONTROL

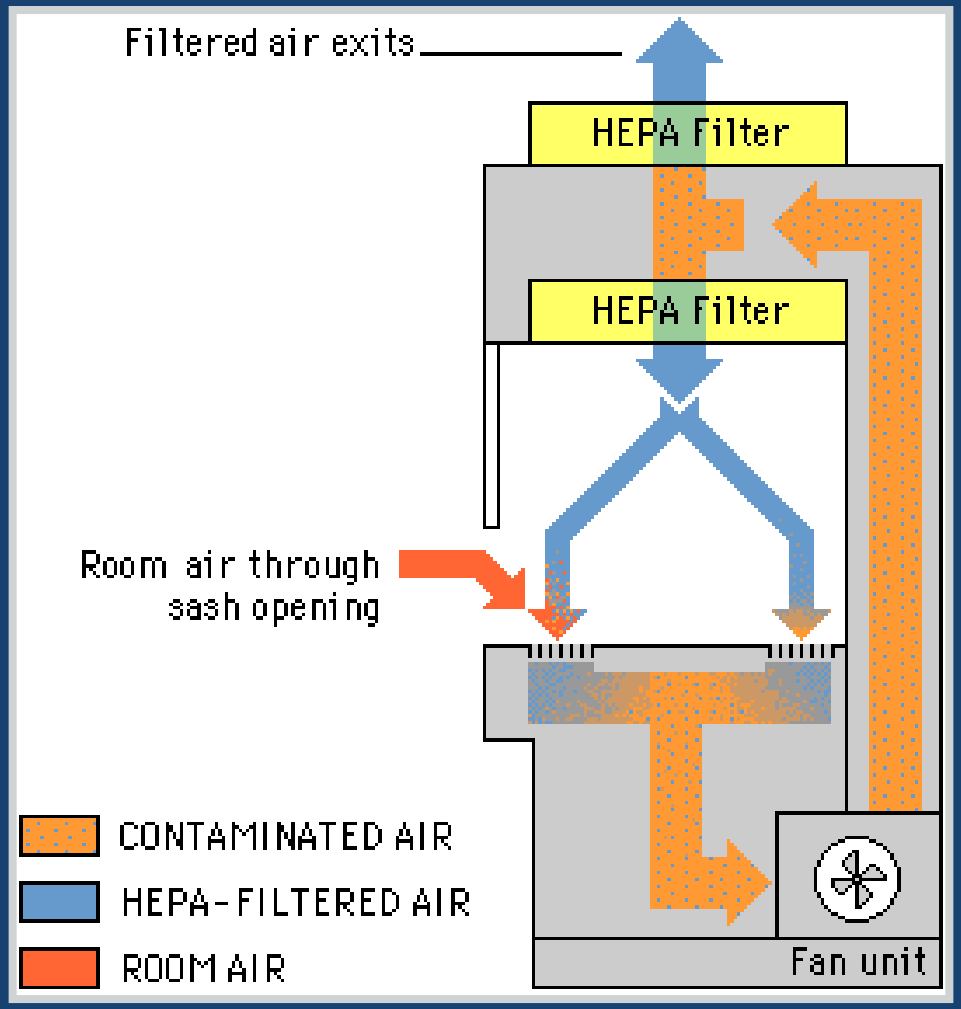
- Aerosol generation
  - Vortexing, centrifuging, expelling pipets
  - Aspirating, removing tops from tubes/flasks
- Minimize exposure to aerosols
  - Use engineering controls
    - » Biosafety Cabinet
  - Wrap tube cap with alcohol-soaked gauze
  - Keep tubes capped
  - Centrifuge safety cups
  - Control potential for splash / splatter
  - Change gloves frequently

USING THE BIOSAFETY CABINET

- Class II BSC provides personnel, environment, and product protection
- Recirculated air
- Keep front, side and back airflow grates clear
- Work 4 inches into cabinet

- Make sure HEPA is working properly
- LIMIT TURBULENCE
  - Blocking air flow
  - Heat sources
  - Rapid movement

AIRFLOW IN A CLASS II BSC



BSC WORK PROTOCOL

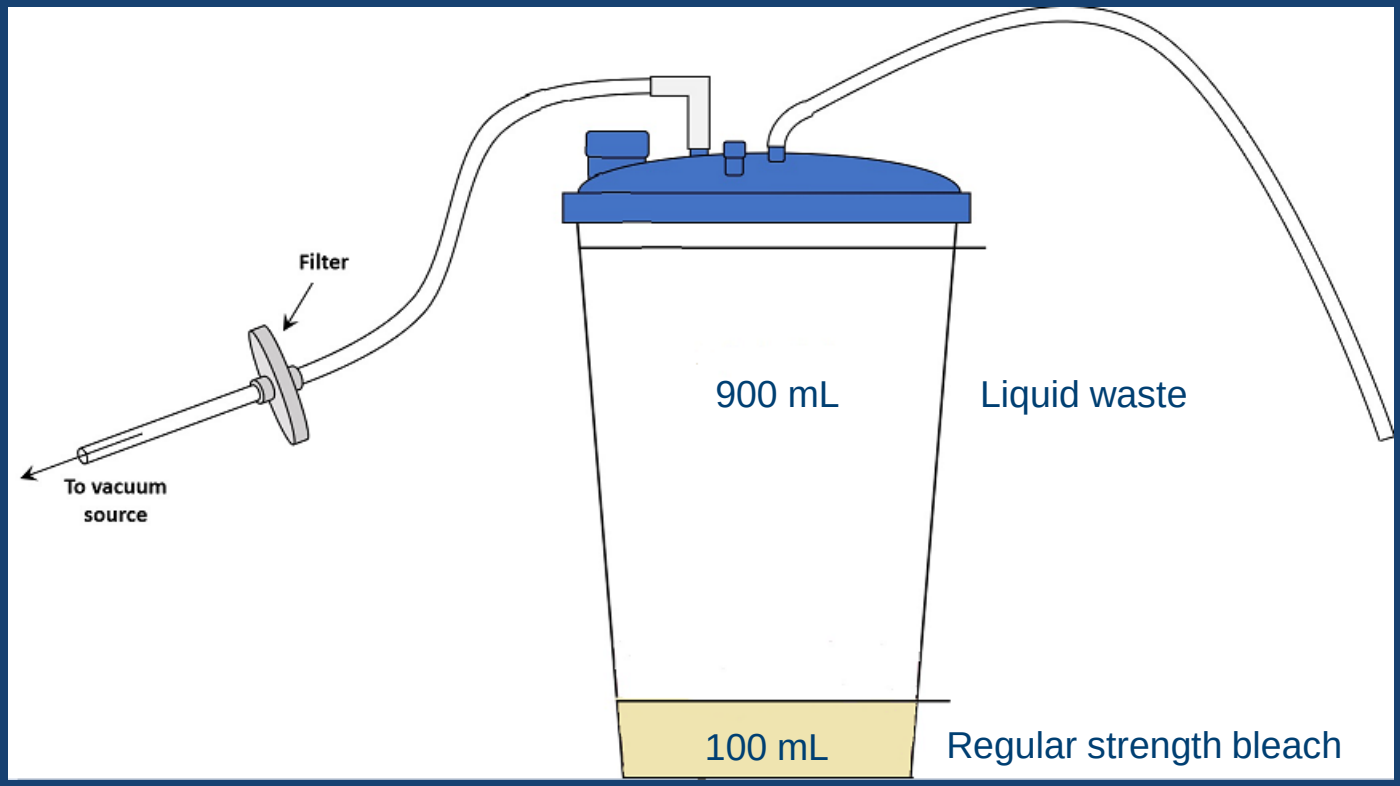
- Wipe down surfaces with disinfectant
- Place supplies in cabinet
- Keep sash below alarm height
- Set up work area from clean to dirty
  - Prevents cross contamination
- Wipe down surfaces with disinfectant when work is complete

USE SHARPS SAFELY

- Dispose of needles/syringes as a unit
  - Avoid handling the needle once it is used
- Do not recap needles
- Do not bend, break or shear a needle
- Use a sheath for scalpels and straight razors
- Dispose of all sharps in puncture resistant sharps containers, labeled with the biohazard symbol
  - Syringes alone are considered sharps in MA
- If storing sharps, use a puncture resistant container

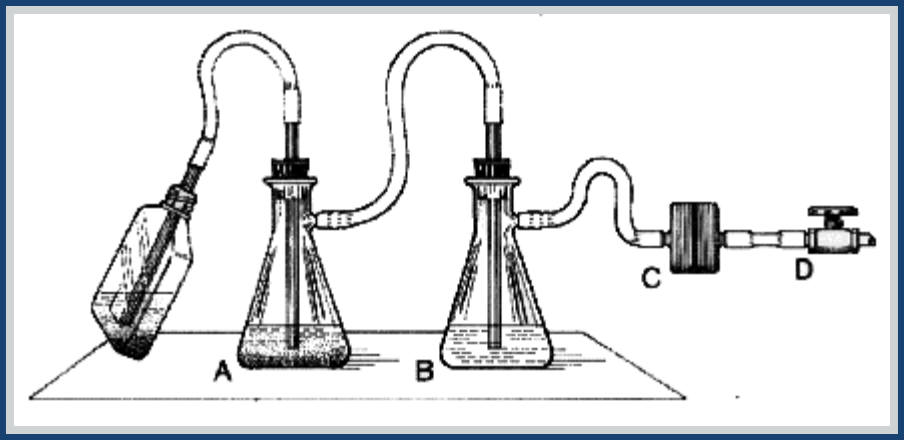
ASPIRATION FLASKS

- Final concentration of 10% bleach (~0.5% sodium hypochlorite) in aspiration flasks



ASPIRATION FILTERS

- Use in-line 0.2 µm (micron) filters to protect the vacuum line
- Once work is completed, aspirate a few mL of disinfectant to clean the line before turning off the vacuum



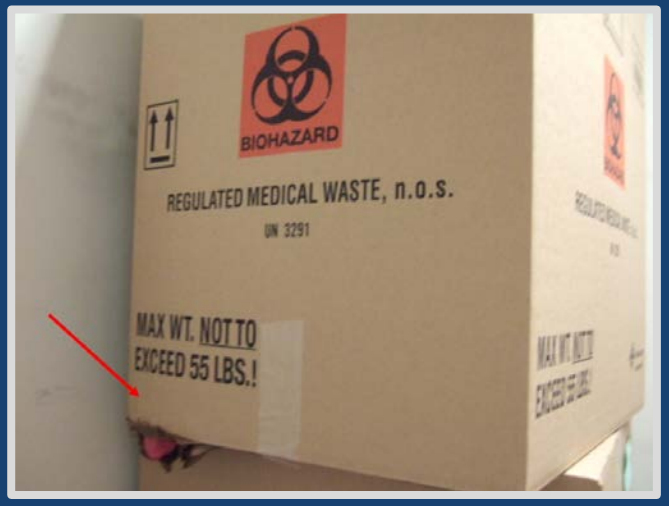
Biohazardous Waste & Disinfection

RED BAG WASTE

- Contaminated plastic and paper items used to work with recombinant Tetrahymena and human cells
  - Petri dishes
  - Plastic containers
  - Conical tubes
  - Test tubes
  - Paper towels/kimwipes
- Items that may puncture the bag (e.g., serological pipettes) must be double bagged or disposed of in a sharps container

RED BAG WASTE

- Biowaste containers must be closed in BSL-2 labs
- Limited liquids (<5ml)
  - Generator is responsible for any leaks during transport
- No free sharps!
- Do not overfill bioboxes
  - 55 lb limit



RED BAG WASTE

- Single knot, no bunny ears

BIOLOGICAL SHARPS WASTE

- Sharps must go in designated sharps containers
  - Needles
  - Syringes
  - Scalpels
  - Razors
  - Pasteur pipets
  - Serological pipettes and tips (best practice)

- NEVER pick up spilled sharps with hands
  - Use scoop/scraper or forceps

DISINFECTION

- Choose the right agent and use the proper contact time!
  - ALL disinfectants must be approved prior to use
    - » There are regulatory requirements
- Surfaces must be disinfected at the end of each work shift and after overt spills
- Equipment must be disinfected prior to service
- Liquid waste must be disinfected before sink disposal
  - Follow established disinfection procedures

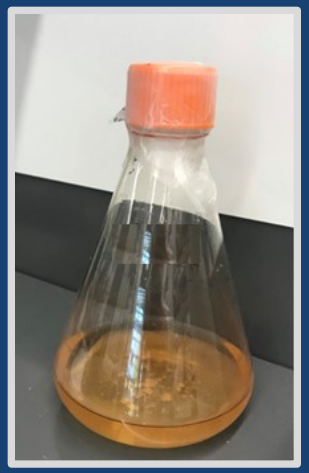
COMMON DISINFECTANTS

- Freshly prepared 10% bleach solutions (0.5% sodium hypochlorite)
  - For general disinfection
  - Contact time is 30 min
  - Regular strength bleach should be stored under lab sinks

- 70% ethanol or 70% isopropanol can be used as a surface disinfectant, but not appropriate for liquid waste

LIQUID WASTE

- All liquid waste must be disinfected before disposal
  - 10% to 20% bleach v/v (final concentration of bleach)
    - Use regular strength bleach (~5% sodium hypochlorite)
      - 10% bleach (~0.5% sodium hypochlorite)
        - 1 part bleach to 9 parts liquid waste
      - 20% bleach (~1% sodium hypochlorite)
        - 2 parts bleach to 8 parts liquid waste



  - 30 minute contact time
  - Sink dispose if no other hazards (e.g., Cadmium) present

CADMIUM CONTAINING CULTURES

- Cadmium is a Chemical Waste and should never go down the drain, in the regular garbage, or in the biohazardous waste stream.
- Disposal of Cadmium cultures*:*
  - Treat with a 10% bleach solution for 30 minutes.
  - After bleach treatment, carefully pour solution into a collection vessel. Smaller, clearly labeled, covered collection vessels are distributed around the laboratory for temporary use.
  - When an experiment is complete transfer the contents of the temporary vessels to the 55 gallon collection drum.

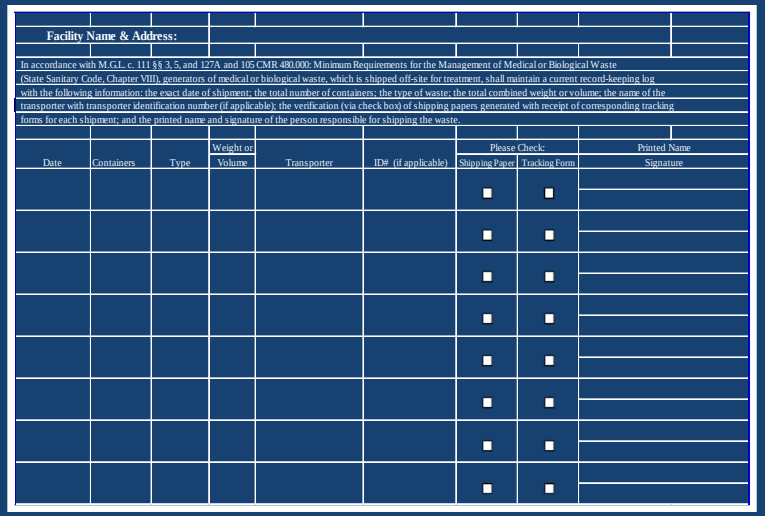
EQUIPMENT DISINFECTION

- Freshly prepared 10% bleach (~0.5% sodium hypochlorite)
- If using on metal, follow with a water or 70% ethanol or 70% isopropanol rinse to reduce corrosion
  - There is a stable 10% bleach product called Bleach-Rite®, which contains a stabilizer
    - Check the expiration date
- 70% ethanol or 70% isopropanol

ALL EQUIPMENT MUST BE DECONTAMINATED BEFORE IT IS SERVICED

105 CMR 480 – SANITARY CODE

- All waste shipped off-site for treatment must be logged
  - Regular removal via licensed waste hauler (Veolia)
- Only DOT/RCRA trained personnel can sign for biohazardous waste shipments
- Waste disposal procedures must be approved by the IBC annually



Facility Name & Address:

In accordance with M.G.L. c. 111 §§ 3, 5, and 127A and 105 CMR 480.000: Minimum Requirements for the Management of Medical or Biological Waste (State Sanitary Code, Chapter VIII), generators of medical or biological waste, which is shipped off-site for treatment, shall maintain a current record-keeping log with the following information: the exact date of shipment; the total number of containers; the type of waste; the total combined weight or volume; the name of the transporter with transporter identification number (if applicable); the verification (via check box) of shipping papers generated with receipt of corresponding tracking forms for each shipment; and the printed name and signature of the person responsible for shipping the waste.

Date	Containers	Type	Weight or Volume	Transporter	ID# (if applicable)	Please Check: Shipping Paper	Please Check: Tracking Form	Printed Name / Signature
						☐	☐	
						☐	☐	
						☐	☐	
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Biohazard Emergencies

BSL-1 SPILLS

- Don lab coat, gloves and safety glasses or goggles
- Surround spill with ring of undiluted regular strength bleach
- Cover spill with paper towels and pour undiluted regular strength bleach over towels to produce an estimated volume to volume concentration of 1:10, bleach to spill ratio
- Allow contact time of 30 minutes
- Wipe up with paper towels
- Follow with soapy water solution and then a final water or 70% ethanol or 70% isopropanol wipe
- Use scoop/scraper for sharps
- All waste from cleanup goes into biohazard waste

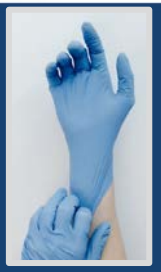
SPILLS IN A BSC

- Continue to let the cabinet run
- Check HEPA operation
- Absorb material with paper towels
- Disinfect surface
- Flood front grill if material spilled into that area
- Drain when 30 minute contact time is complete
- Rinse with water to prevent corrosion

BSL-2 SPILLS OUTSIDE OF A BSC

- Leave area quickly, allow aerosols to settle for 30 minutes
  - Aerosols settling will present contact exposure if spill is cleaned immediately
- Decontaminate clothing using the autoclave or dispose of as biohazard waste

BSL-2 SPILLS OUTSIDE OF A BSC



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- Allow 30 minutes contact time
- Wipe up with paper towels
- Follow with soapy water solution and then a final water or 70% ethanol or 70% isopropanol wipe
- Use scoop/scraper for sharps
- All waste from cleanup goes into biohazard waste
  - Sharps go in sharps container

LARGE SCALE SPILLS (> 10 LITERS)

- Wash hands and exposed skin immediately if you have been exposed to the spill
- Leave the laboratory and evacuate all personnel from the laboratory. Close the door and post a "no entry" sign
- Contact the Biosafety Officer and Emergency Coordinator to plan the cleanup, including notification to Veolia
- Veolia will clean all large scale spills
- The Biosafety Officer or designee will determine if there is a need to call the local Arlington Board of Health

OVERT EXPOSURE

- Needlestick or sharps injury
  - Wash the wound immediately with soap and water
  - Notify your supervisor
  - Go to Occupational Health or ER
  - Fill out Incident Report

- Splash/splatter into eyes, nose, mucous membranes, compromised skin
  - Flush immediately with water
  - Notify your supervisor
  - Follow advice of Occ Health or go to ER
  - Fill out Incident Report

EVALUATION AND TREATMENT

Mt. Auburn Occupational Health Center
725 Concord Avenue
Suite 5100
Cambridge, MA 02138

8:00 AM -12:00 PM
1:00 PM - 4:00 PM

Phone: 617-354-0546
Fax: 617-868-4497

Mt. Auburn Hospital Emergency Department

330 Mount Auburn St.

Cambridge, MA 02318

Anytime

Phone: 617-492-3500

ALWAYS call ahead
Leave a message after hours

OFF HOURS EMERGENCIES

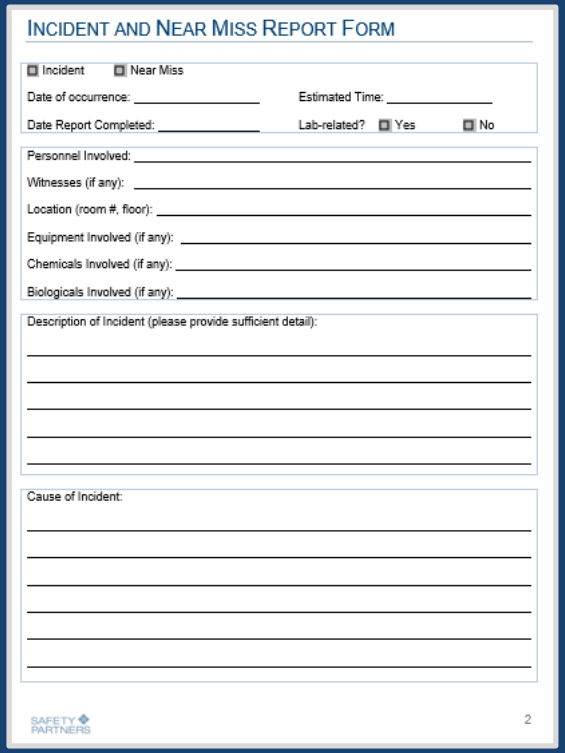
- If medical treatment is needed evenings, nights, weekends, or holidays, seek treatment at ER
- Will provide post-exposure treatment for occupational exposures
- Occupational Health must be notified and will then follow-up on the next working day

WHEN SHOULD I BE EVALUATED?

- Guidance from a health care provider should be sought immediately after suspected exposure
- Some serious exposures may require the initiation of drug therapies that are believed to be most effective when given within a couple hours of the exposure
  - Consultation
  - Postexposure prophylaxis (PEP) regimens
  - Recent developments in treatment and evaluation
    - » Example HCV

INCIDENT REPORT

- Fill out an Incident Report for all biological spills and exposures
- All needle sticks and exposures must be reported immediately
  - The Biosafety Officer completes a needlestick log



INCIDENT AND NEAR MISS REPORT FORM

☐ Incident ☐ Near Miss

Date of occurrence: _____ Estimated Time: _____

Date Report Completed: _____ Lab-related? ☐ Yes ☐ No

Personnel Involved: _____

Witnesses (if any): _____

Location (room #, floor): _____

Equipment Involved (if any): _____

Chemicals Involved (if any): _____

Biologicals Involved (if any): _____

Description of Incident (please provide sufficient detail):

Cause of Incident:

SAFETY PARTNERS

2

Bloodborne Pathogens
29 CFR 1910.1030

WHAT ARE BLOODBORNE PATHOGENS (BBP)?

- Pathogenic microorganisms that are present in human blood and can cause disease in humans
- These pathogens include, but are not limited to, hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV)
- BBP are found in blood, blood products or OPIM (Other Potentially Infectious Materials)

OPIM (OTHER POTENTIALLY INFECTIOUS MATERIALS)

- OPIM include the following human body fluids:
  - Semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, pericardial fluid, peritoneal fluid, amniotic fluid, saliva in dental procedures, any body fluid that is visibly contaminated with blood, and all body fluids in situations where it is difficult or impossible to differentiate between body fluids

OPIM (OTHER POTENTIALLY INFECTIOUS MATERIALS)

- OPIM also include:

- Any unfixed tissue or organ (other than intact skin) from a human (living or dead)
- HIV-containing cell or tissue cultures, organ cultures, and HIV- or HBV-containing culture medium or other solutions
- Blood, organs, or other tissues from experimental animals infected with HIV or HBV

THE REGULATION

- OSHA Standard 29 CFR 1910.1030 (Bloodborne Pathogens)
  - https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1030
- Implemented in 1992
- Applies to all occupational exposure to blood or OPIM
  - Occupational exposure means reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or OPIM that may result from the performance of an employee's duties

EXPOSURE CONTROL PLAN (ECP)

- Each employer covered under the BBP Standard shall establish a written Exposure Control Plan designed to eliminate or minimize employee exposure
- The ECP for AbCellera Boston can be found on the safety shelf in the main lab (included in the Biosafety Manual & Exposure Control Plan)

CONTENT OF THE EXPOSURE CONTROL PLAN (ECP)

Exposure determination

The schedule and method of implementation for:

- Methods of compliance
- HIV and HBV research laboratories and production facilities
- Hepatitis B vaccination and post-exposure evaluation and follow-up
- Communication of hazards to employees
- Recordkeeping
- The procedure for the evaluation of circumstances surrounding exposure incidents

EXPOSURE DETERMINATION

- Employees of the following departments may have exposure to human source materials:
  - Genetics
  - Immunology
  - Molecular Biology
- Job classifications in which some or all employees in those job classifications can have occupational exposure:
  - Research Associate
  - Research Scientist I
  - Research Scientist II
  - Head of Protein Expression and Genetics
  - Senior Vice President, Research

EXPOSURE DETERMINATION

- Tasks and procedures or groups of closely related tasks and procedures in which occupational exposure can occur:
  - Work with human cell lines and primary human cells
  - Shipping or receiving human source materials
  - Closing up, boxing or moving biomedical waste containers

BLOODBORNE PATHOGENS

- Main BBPs of Concern
  - Hepatitis B Virus (HBV)
  - Hepatitis C Virus (HCV)
  - Human Immunodeficiency Virus (HIV)
- All are bloodborne viruses
- Can produce chronic infection
- Documented cases establish that transmission is possible in healthcare settings and in laboratories

HEPATITIS B

- The hepatitis B virus (HBV) causes hepatitis B, an inflammatory infection of the liver
- Complications can lead to cirrhosis (scarring), liver cancer, and liver failure

HEPATITIS B

- Hepatitis B infections can be acute or chronic
  - Acute: an infection that occurs within the first 6 months after someone is exposed to the virus, with or without symptoms. An asymptomatic person can still pass the virus to others. Some people are able to clear the virus without treatment.
  - Chronic: long-term illness when the virus remains in a person's body for more than 6 months. Less than 10% of healthy adults who are infected will develop a chronic infection. Chronic hepatitis B is a serious disease that can lead to long-term health problems, and even death.

HEPATITIS B SYMPTOMS

Only about 30-50% of adult acute hepatitis B infections may exhibit clinical symptoms

Symptoms may include:

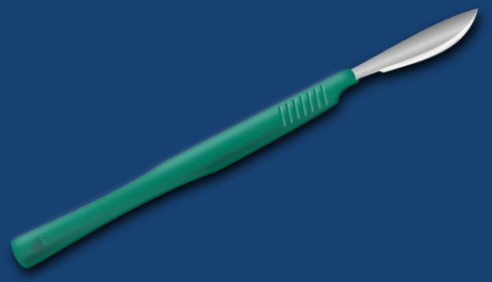
- Loss of appetite
- Abdominal discomfort or pain
- Nausea and vomiting
- Jaundice or yellowing of the skin and eyes
- Fever
- Fatigue
- Joint pain
- Dark urine
- Grey-colored stool

HEPATITIS B STATISTICS

- In 2018, a total of 3,322 cases of acute hepatitis B were reported to the CDC
  - The CDC estimates the actual number of cases in 2018 to be almost 21,600
- In the United States, an estimated 862,000 people have chronic hepatitis B, but the number is likely higher
- 1,649 deaths related to hepatitis B were reported in 2018 in the US, this is likely underestimated
- Worldwide there are approximately 257 million people with hepatitis B

HBV - OCCUPATIONAL TRANSMISSION

- Hepatitis B transmission in the workplace:
  - Percutaneous injury
    - Example: puncture wounds or cut from a needle or other sharp object
    - Transmission rate is 6-30% for percutaneous exposure from known positive sources



HBV - OCCUPATIONAL TRANSMISSION

- Hepatitis B transmission in the workplace:
  - Contact with mucous membrane or nonintact skin
    - Examples: chapped, abraded skin, or skin affected by dermatitis
  - Indirect exposure from contaminated objects
    - The hepatitis B virus can remain infectious on environmental surfaces for up to a week (7 days) in a dry state

HBV VACCINATION

A safe and effective vaccine against hepatitis B is available to those potentially at risk

- Non-infectious recombinant vaccine made in yeast cells

The vaccine is provided free of charge to all employees affected by the Standard, even if you declined initially

- This vaccination must be offered after the worker has received the required bloodborne pathogens training and within 10 days of initial assignment to a job with occupational exposure

Three shot series

(other options may be available)

- Titer (blood test) available after the series to confirm that the person has developed immunity against HBV

HEPATITIS C

- The hepatitis C virus (HCV) causes hepatitis C, an inflammatory infection of the liver
- Complications can lead to cirrhosis (scarring), liver cancer, and liver failure
- There is no vaccine for hepatitis C
  - Treatment is available

HEPATITIS C

- Hepatitis C infections can be acute or chronic
  - Acute: an infection that occurs within the first 6 months after someone is exposed to the virus. An asymptomatic person can still pass the virus to others. Some people are able to clear the virus without treatment.
  - Chronic: long-term illness when the virus remains in a person's body for more than 6 months. 55-85% of people who become infected with the hepatitis C virus will develop a chronic infection. Chronic hepatitis C is a serious disease that can lead to long-term health problems, and even death if left untreated.

HEPATITIS C SYMPTOMS

Only about 20-30% of adult acute hepatitis C infections may exhibit clinical symptoms

Symptoms may include:

- Loss of appetite
- Abdominal discomfort or pain
- Nausea and vomiting
- Jaundice or yellowing of the skin and eyes
- Fever
- Fatigue
- Joint pain
- Dark urine
- Grey-colored stool

HEPATITIS C STATISTICS

- Most common chronic bloodborne infection in United States
- An estimated 3.5 million Americans have chronic hepatitis C infection
- 40% of chronic liver disease is HCV-related, leading to more than 15,000 deaths annually
- HCV-associated end-stage liver disease is the most common indication for liver transplants in U.S. adults

HCV - OCCUPATIONAL TRANSMISSION

Hepatitis C transmission in the workplace:

- Percutaneous injury
  - Examples: puncture wounds or cut from a needle or other sharp object
  - Transmission rate is about 2% for percutaneous exposure to known positive sources

Risk factors for occupational transmission of hepatitis C are not well defined

Environmental transmission is not believed to be important

HCV rapidly degrades at room temperature

HUMAN IMMUNODEFICIENCY VIRUS (HIV)

- HIV is a virus that attacks the body's immune system, specifically the CD4 T-cells
- Damages to the immune system makes it harder for the body to fight off infections and other diseases
- If not treated, HIV infections generally lead to AIDS (Acquired Immunodeficiency Syndrome)
  - Secondary infection by opportunistic pathogens or cancers due to very weak immune system
- There is no vaccine or cure for HIV infection
  - Treatment is available

HIV INFECTION AND SYMPTOMS

Stage 1: Acute Infection

- Within 2 to 4 weeks after infection, about 2/3 of people will have a flu-like illness. Symptoms can last from a few days to several weeks. Some people will be asymptomatic.

Symptoms may include:

- Fever
- Chills
- Rash
- Night sweats
- Muscle aches
- Sore throat
- Fatigue
- Swollen lymph nodes
- Mouth ulcers

HIV INFECTION AND SYMPTOMS

Stage 2: Clinical Latency (Chronic Infection)

- The virus multiplies at low levels
- People may be asymptomatic
  - If viral load is detectable, people can still transmit HIV during this stage, even if asymptomatic
- Without treatment, people may be in this stage for 10-15 years

HIV INFECTION AND SYMPTOMS

Stage 3: AIDS

- The virus weakens the body's immune system and progression to AIDS (acquired immunodeficiency syndrome) takes place

Symptoms may include:

- Rapid weight loss
- Recurring fever or profuse night sweats
- Extreme and unexplained tiredness
- Prolonged swelling of the lymph glands in the armpits, groin, or neck
- Diarrhea that lasts for more than a week
- Pneumonia
- Red, brown, pink, or purplish blotches on or under the skin or inside the mouth, nose, or eyelids
- Memory loss, depression, and other neurologic disorders

HIV STATISTICS

- At the end of 2019, an estimated 1,189,700 people in the United States had HIV
  - About 13% did not know they had HIV
- Worldwide in 2020
  - Roughly 1.5 million new cases of HIV
  - Approximately 37.7 million living with HIV
  - Estimated 680,000 AIDS-related deaths

HIV - OCCUPATIONAL TRANSMISSION

- HIV transmission in the workplace:
  - Percutaneous injury
    - Examples: puncture wounds or cut from a needle or other sharp object
    - Transmission rate is 0.3% for percutaneous exposure to known positive sources

HIV - OCCUPATIONAL TRANSMISSION

- HIV transmission in the workplace:
  - Contact with mucous membrane
    - Transmission rate is 0.1% for mucous membrane exposure to known positive sources
  - Contact with nonintact skin (examples: chapped, abraded skin, or skin affected by dermatitis)
    - Transmission rate is < 0.1% for nonintact skin exposure to known positive sources

HIV - OCCUPATIONAL TRANSMISSION

- U.S. healthcare personnel (1985-2013)
  - 58 documented cases
    - HIV negative at time of exposure and became HIV positive during follow-up period
  - 150 possible other cases
    - No documented exposure and no known risk factor for HIV infection
- One confirmed occupational case reported to the CDC since 1999

HIV - OCCUPATIONAL TRANSMISSION DOCUMENTED CASES (N=58)

- 51 (88%) involved percutaneous exposures
  - Latest case in 2008 was a laboratory technician sustaining a needlestick while working with a live HIV culture
- 5 mucocutaneous exposures
- 2 exposure route unknown

POSSIBLE BBP EXPOSURE AT ABCELLERA BOSTON

- Human cell lines
- Primary human cells
  - Peripheral blood mononuclear cells (PBMCs)

HUMAN CELL LINES > BSL-2!

- OSHA Clarification
  - If they are capable of propagating viruses, they are considered OPIM under the law unless they have been tested, shown to be free of ALL human pathogens and documented as such by the institution
- They must be manipulated at BSL-2
- ATCC does not test cell lines for all pathogens

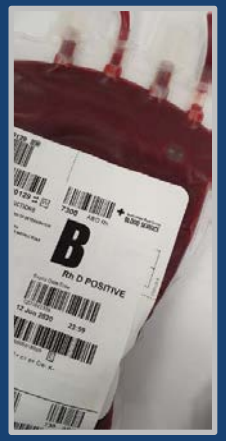
See the OSHA letter of interpretation at:
http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=INTERPRETATIONS&p_id=21519
See the double asterisk at the bottom of the letter.

UNIVERSAL PRECAUTIONS

- An approach to infection control and the backbone of the Bloodborne Pathogens Standard
- All human blood and other potentially infectious materials are treated as if known to be infectious for HIV, HBV, HCV, and other bloodborne pathogens
- Under circumstances in which differentiation between body fluid types is difficult or impossible, all body fluids shall be considered potentially infectious materials

WHY FOLLOW UNIVERSAL PRECAUTIONS?

- You don’t want to assume any human source material is free of pathogens
- Example: working with human blood from outside vendor
  - Donors screened initially and periodically
  - Original screen may be clean, subsequent screens can come back positive for bloodborne pathogens
    - It may take several weeks after exposure for someone to develop antibodies



SELF DISCLOSURE

- From the BMBL 6th Edition published by the CDC and NIH:
  - Personal health status may affect an individual's susceptibility to infection and ability to receive available immunizations or prophylactic interventions
  - Therefore, all personnel, and particularly those of reproductive age and/or those having conditions that may predispose them to increased risk for infection (e.g., organ transplant, medical immunosuppressive agents), are provided information regarding immune competence and susceptibility to infectious agents
  - Individuals having such conditions are encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance

EXPOSURE ROUTES FOR BLOODBORNE PATHOGENS

- Accidents with sharps (puncture wounds)
- Improper material handling
- Exposed, non-intact (broken) skin
- No gloves or defective gloves
- Eating, drinking, applying cosmetics in the laboratory
- Incomplete disinfection of materials
- Overt exposures to aerosols or splashes

PREVENTING TRANSMISSION OF BLOODBORNE PATHOGENS

- Treat all human source material, including cell lines, as potentially infectious
- Use barriers to prevent contact
- Prevent percutaneous injuries
- Safely dispose of sharps and contaminated materials
- Promote hepatitis B vaccination
- Use BSL-2 practices when working with human materials

SAFER ENGINEERED SHARPS

- If you utilize a sharp with human source material, the safest engineered sharp available on the market will be provided to make your work easier and with less risk
  - Examples: retractable needles, self sheathing scalpels
- If you know of a product that you would like to use, notify your supervisor with the product information

SAFER SHARPS

- It is an OSHA bloodborne pathogens requirement to evaluate safer engineered sharps for lab use

- End user input on the use of needles, scalpels, razors or any sharps with human materials is essential
  - A review of new safer sharps options must take place annually and be documented

CONCLUSION

- You are at risk for occupational exposure to Bloodborne Pathogens in the laboratory
- The Exposure Control Plan outlines the necessary steps to reduce infection risk
  - If you would like a copy of the ECP, contact the Biosafety Officer
- When accidents occur, prompt medical attention is necessary
  - The CDC recommends treatment within 2 hours
- Prevention is the key

QUESTIONS?

Thank you!

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BIOSAFETY MANUAL & EXPOSURE CONTROL PLAN

ABCELLERA BOSTON

91 MYSTIC STREET

ARLINGTON, MA 02474

MAY, 2023

SAFETY PARTNERS

Hands-on Workplace Safety

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BIOSAFETY MANUAL & EXPOSURE CONTROL PLAN

The following Biosafety Manual & Exposure Control Plan dated May 2023 has been approved, as written, by:

Biosafety Officer

Signature: _____ Date: _____

Print Name: May 2023

CONTENTS

1. INTRODUCTION

Purpose

AbCellera Boston is committed to the prevention of employee exposures to biohazardous materials because of their job requirements. To reduce or eliminate the hazards of occupational exposure, the company has implemented this Biological Safety Manual & Exposure Control Plan (ECP) to provide details on safety guidelines and employee protection measures. This manual explains the use of various engineering and work practice controls, including the use of personal protective equipment, housekeeping requirements, medical surveillance, and hepatitis B vaccination programs as they apply to the work done onsite. Also addressed is how the existence of hazards to employees is communicated, including labels and signs, recordkeeping, and training.

This plan was developed in accordance with the OSHA "Occupational Exposure to Bloodborne Pathogens: Final Rule" in 29 CFR 1910.1030, to minimize or eliminate employee exposure to bloodborne pathogens and other biological hazards. A copy of this OSHA Standard is located in the central safety files and online at www.osha.gov.

This manual applies to laboratory research and support activities that may involve exposure to biohazardous agents or materials, and that come under the purview of the Biological Safety Officer. The manual is intended to give an overview of biological safety and to provide compliance with the OSHA Bloodborne Pathogens Standard. It is not meant to be an extensive guide for experiment-specific processes or provide specific safety protocols for all biological materials. In these cases, the Biological Safety Officer must perform a specific Job Safety Analysis or risk assessment that results in written procedures and training. This information can then be added to this manual as appendices or kept separately in the safety files.

Terms used in this manual are defined in Appendix I.

2. RESPONSIBILITIES

Biological Safety Officer (BSO)

As an official representative of the company, the Biological Safety Officer has biological safety overview of all ongoing scientific projects at AbCellera Boston. The BSO will provide guidance to all Principal Investigators, Supervisors, and Employees of laboratories performing biological work.

The BSO will ensure compliance with the Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH) publications, *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) and the *Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, as appropriate. The BSO will ensure adherence and compliance with any local regulations regarding biological safety.

The BSO will be an active participant on the Safety Committee and Institutional Biosafety Committee (IBC).

The BSO or designee will conduct an annual review and update of this manual. This will include information that reflects any changes in technology that eliminates or reduces occupational exposure by:

- Implementing a safer sharps program that evaluates laboratory innovations and technological developments that reduce the risk of exposure, particularly medical devices designed to reduce needlesticks
- Documenting the consideration and use of appropriate, commercially available, and effective safer devices by describing the devices identified as candidates for use, the method used to evaluate those devices, and the justification for the eventual selection. The documentation can be accomplished by listing the employees involved and describing the process by which input was requested; or through other documentation, including references to the minutes of meetings, copies of documents used to request employee participation, or records of responses received from employees.

Principal Investigator (PI)

A PI will ensure compliance with the Arlington Board of Health, NIH guidelines, and OSHA regulations, when work with regulated biological agents such as recombinant DNA, human source materials, or other potentially infectious materials (OPIM) is conducted. The PI will register all work involving recombinant or synthetic nucleic acid molecules with the Institutional Biosafety Committee (IBC) Chairperson.

The PI that oversees a project will ensure that all employees have project specific training for each experiment. The PI must ensure biological and physical containment conditions are maintained, such as strain or phenotype purity, proper practices, techniques, and equipment. Other responsibilities can be found in section IV-B-7-a of the NIH guidelines.

Supervisors

Supervisors will assess all potentially hazardous agents involved in work activities within their laboratories and institute appropriate safeguards. Supervisors will have experiment-specific protocols for biohazardous work which include measures for minimizing exposure incidents, informing personnel of potential hazards and the basis for assessing hazards, assuring proficiency of staff, and maintaining and updating these protocols on a continuing basis.

Supervisors will ensure that their employees receive the proper training, follow all safety policies, report incidents and correct non-compliance issues as indicated by the BSO or Safety Committee. Supervisors must also ensure that all employees with the potential for occupational exposure to bloodborne pathogens follow the provisions of this plan and manual. This includes providing a copy of this Biological Safety Manual & Exposure Control Plan to those employees, requiring that they attend an initial and annual training session, enforcing compliance with this plan, ensuring that new employees who will have occupational exposure are properly trained, and performing follow-up procedures for all exposure incidents.

It is recommended that all supervisors inform the BSO before the acquisition/ordering of any potentially biohazardous material.

Project Manager

The Project Manager is responsible for ensuring biosafety cabinets are certified on an annual basis.

Employees

Employees are to perform tasks and procedures in a manner that minimizes or eliminates their own and others' exposure and to perform duties as established in this Biological Safety Manual & Exposure Control Plan and as trained. It is the employee's responsibility to report any incidents, accidents, exposures, or needlesticks to their supervisor and the BSO immediately. All incidents must be documented by the employee on an incident report within 24 hours.

3. RISK GROUPS

The American Biological Safety Association (ABSA, https://ABSA.org/), NIH, and the Canadian Laboratory Biosafety Guidelines have categorized risk group for biological organisms.

Risk Group 1: Low Individual and Community Risk

A biological agent:

- That is well-characterized and not known to consistently cause disease in immunocompetent adult humans
- That presents minimal potential hazard to laboratory personnel and the environment

Risk Group 2: Moderate Individual Risk, Limited Community Risk

A biological agent:

- That can cause human disease and might be a moderate hazard to workers
- That is unlikely to spread to the community
- For which there is usually effective prophylaxis or treatment available

Risk Group 3: High Individual Risk, Low Community Risk

A biological agent:

- That can cause severe or lethal human disease and present a serious hazard to workers
- That may present a risk of spreading to the community
- For which there may be effective prophylaxis or treatment available

Risk Group 4: High Individual Risk, High Community Risk

A biological agent:

- That causes severe or lethal human disease and is a serious hazard to workers
- That may present a high risk of spreading to the community
- For which there is usually no effective prophylaxis or treatment available

Risk Assessment

To assess a biohazard and provide adequate containment, it is necessary to identify the risk group of an organism and then perform a risk assessment of the experimental situation. At a minimum, five factors must be considered to assess occupational risk while working with biohazardous materials and to understand what types of containment are necessary:

- What is the infectious dose of the organism?
- What is the virulence of the organism?
- What are the likely routes of entry?
- What is the viability of the organism in specific environments?
- Are suitable disinfectants available for the organism?
- Is effective prophylaxis available?

When cell cultures are known to contain an etiologic agent, an oncogenic virus, or amphotropic packaging system, the cell line must be classified at the same level as that recommended for the agent. This is the same for all cell cultures purposely inoculated with an infectious agent. An example is immortalized cells (also known as continuous cell lines). These are obtained by isolating cells from tumors, by mutating primary cells with mutagens, or using viruses or rDNA to generate indefinitely growing cells. Hybridoma cell lines are immortalized cell lines created by fusion of primary cells with a continuous cell line. In general, primary cell cultures are less characterized than immortalized cell lines and are not typically tested for contaminating pathogens. Tumorigenic potential is a risk to consider with immortalized cell lines.

4. BIOSAFETY CONTAINMENT LEVELS

After a risk assessment is performed as described in section 3, a physical containment level is assigned to the work being performed with that organism. It is important to note that although risk group and biosafety level often coincide (i.e., risk group 1 organisms are handled at biosafety level 1), this is not always the case. Only a full risk assessment can determine the containment level for each biological agent in use in the laboratory.

Four levels of biosafety controls have been defined by the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH). They are combinations of laboratory practices, techniques, safety equipment and the physical design of the laboratory facility. Experience has shown that strict adherence to these guidelines contributes to a healthier and safer environment, both in the workplace and in the surrounding community.

Biosafety physical containment levels and related safety practices may be applied to work with all types of biohazardous materials, such as genetically manipulated cell lines, potentially infectious human or animal body fluids and tissues, bacterial or viral cultures and live animals.

An in-depth description of biosafety containment levels 1 and 2 is given below because these are the two levels most used. These descriptions are taken directly from the CDC/NIH publication Biosafety in Microbiological and Biomedical Laboratories (BMBL) found at https://www.cdc.gov/labs/BMBL.html. A table which summarizes the basics of all four biosafety levels is provided in Appendix II, and detailed information on BSL-3 and BSL-4 can be found in the BMBL. The information specific to AbCellera Boston can be found in the other sections of this manual.

Biosafety Level 1 (BSL-1)

Biosafety Level 1 is suitable for work involving well-characterized agents not known to consistently cause disease in immunocompetent adult humans, and present minimal potential hazard to laboratory personnel and the environment. BSL-1 laboratories are not necessarily separated from the general traffic patterns in the building. Work is typically conducted on open bench tops using standard microbiological practices. Special containment equipment or facility design is not required but may be used as determined by appropriate risk assessment. Laboratory personnel must have specific training in the procedures conducted in the laboratory and must be supervised by a scientist with training in microbiology or a related science.

The following standard practices, safety equipment, and facility requirements apply to BSL-1:

Standard Microbiological Practices

- The laboratory supervisor enforces the institutional policies that control safety in and access to the laboratory.
- The laboratory supervisor ensures that laboratory personnel receive appropriate training regarding their duties, potential hazards, manipulations of infectious agents, necessary precautions to minimize exposures, and hazard/exposure evaluation procedures (e.g.,

physical hazards, splashes, aerosolization) and that appropriate records are maintained. Personnel receive annual updates and additional training when equipment, procedures, or policies change. All persons entering the facility are advised of the potential hazards, are instructed on the appropriate safeguards, and read and follow instructions on practices and procedures. An institutional policy regarding visitor training, occupational health requirements, and safety communication is considered.

- Personal health status may affect an individual's susceptibility to infection and ability to receive available immunizations or prophylactic interventions. Therefore, all personnel, and particularly those of reproductive age and/or those having conditions that may predispose them to increased risk for infection (e.g., organ transplant, medical immunosuppressive agents), are provided information regarding immune competence and susceptibility to infectious agents. Individuals having such conditions are encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.
- A safety manual specific to the facility is prepared or adopted in consultation with the facility director and appropriate safety professionals. The safety manual is available, accessible, and periodically reviewed and updated, as necessary.
    - The safety manual contains sufficient information to describe the biosafety and containment procedures for the organisms and biological materials in use, appropriate agent-specific decontamination methods, and the work performed.
    - The safety manual contains or references protocols for emergency situations, including exposures, medical emergencies, facility malfunctions, and other potential emergencies. Training in emergency response procedures is provided to emergency response personnel and other responsible staff according to institutional policies.
- A sign is posted at the entrance to the laboratory when infectious materials are present. Posted information includes: the laboratory's Biosafety Level, the supervisor's or other responsible personnel's name and telephone number, PPE requirements, general occupational health requirements (e.g., immunizations, respiratory protection), and required procedures for entering and exiting the laboratory. Agent information is posted in accordance with the institutional policy.
- Long hair is restrained so that it cannot contact hands, specimens, containers, or equipment.
- Gloves are worn to protect hands from exposure to hazardous materials.
    - Glove selection is based on an appropriate risk assessment.
    - Gloves are not worn outside the laboratory.
    - Change gloves when contaminated, glove integrity is compromised, or when otherwise necessary.
    - Do not wash or reuse disposable gloves, and dispose of used gloves with other contaminated laboratory waste.

- Gloves and other PPE are removed in a manner that minimizes personal contamination and transfer of infectious materials outside of the areas where infectious materials and/or animals are housed or manipulated.
- Persons wash their hands after working with potentially hazardous materials and before leaving the laboratory.
- Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption are not permitted in laboratory areas. Food is stored outside the laboratory area.
- Mouth pipetting is prohibited. Mechanical pipetting devices are used.
- Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassware are developed, implemented, and followed; policies are consistent with applicable state, federal, and local requirements. Whenever practical, laboratory supervisors adopt improved engineering and work practice controls that reduce risk of sharps injuries. Precautions are always taken with sharp items. These include:
    - Plasticware is substituted for glassware whenever possible.
    - Use of needles and syringes or other sharp instruments is limited in the laboratory and is restricted to situations where there is no alternative (e.g., parenteral injection, blood collection, or aspiration of fluids from laboratory animals or diaphragm bottles). Active or passive needle-based safety devices are to be used whenever possible.
        - Uncapping of needles is performed in such a manner to reduce the potential for recoil causing an accidental needlestick.
        - Needles are not bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
        - If absolutely necessary to remove a needle from a syringe (e.g., to prevent lysing blood cells) or recap a needle (e.g., loading syringes in one room and injecting animals in another), a hands-free device or comparable safety procedure must be used (e.g., a needle remover on a sharps container, the use of forceps to hold the cap when recapping a needle).
        - Used, disposable needles and syringes are carefully placed in puncture-resistant containers used for sharps disposal immediately after use. The sharps disposal container is located as close to the point of use as possible.
    - Non-disposable sharps are placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving.
    - Broken glassware is not handled directly. Instead, it is removed using a brush and dustpan, tongs, or forceps.
- Perform all procedures to minimize the creation of splashes and/or aerosols.

- Decontaminate work surfaces after completion of work and after any spill or splash of potentially infectious material with appropriate disinfectant. Spills involving infectious materials are contained, decontaminated, and cleaned up by staff who are properly trained and equipped to work with infectious material. A spill procedure is developed and posted within the laboratory.
- Decontaminate all cultures, stocks, and other potentially infectious materials before disposal using an effective method, consistent with applicable institutional, local, and state requirements. Depending on where the decontamination will be performed, the following methods are used prior to transport:
    - Materials to be decontaminated outside of the immediate laboratory are placed in a durable, leak-proof container and secured for transport. For infectious materials, the outer surface of the container is disinfected prior to moving materials and the transport container has a universal biohazard label.
    - Materials to be removed from the facility for decontamination are packed in accordance with applicable local, state, and federal regulations.
- An effective integrated pest management program is implemented.
- Animals and plants not associated with the work being performed are not permitted in the laboratory.

Special Practices

None required.

Safety Equipment (Primary Barriers and Personal Protective Equipment)

- Special containment devices or equipment, such as biosafety cabinets (BSCs), are not generally required.
- Protective laboratory coats, gowns, or uniforms are worn to prevent contamination of personal clothing.
- Protective eyewear is worn by personnel when conducting procedures that have the potential to create splashes and sprays of microorganisms or other hazardous materials. Eye protection and face protection are disposed of with other contaminated laboratory waste or decontaminated after use.
- In circumstances where research animals are present in the laboratory, the risk assessment considers appropriate eye, face, and respiratory protection, as well as potential animal allergens.

Laboratory Facilities (Secondary Barriers)

- Laboratories have doors for access control.
- Laboratories have a sink for handwashing.
- An eyewash station is readily available in the laboratory.

- The laboratory is designed so that it can be easily cleaned.
    - Carpets and rugs in laboratories are not appropriate.
    - Spaces between benches, cabinets, and equipment are accessible for cleaning.
- Laboratory furniture can support anticipated loads and uses.
    - Benchtops are impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals.
    - Chairs used in laboratory work are covered with a non-porous material that can be easily cleaned and decontaminated with appropriate disinfectant.
- Laboratory windows that open to the exterior are fitted with screens.
- Illumination is adequate for all activities and avoids reflections and glare that could impede vision.

Biosafety Level 2 (BSL-2)

Biosafety Level 2 builds upon BSL-1. BSL-2 is suitable for work involving agents that pose moderate hazards to personnel and the environment. It differs from BSL-1 in that 1) laboratory personnel have specific training in handling pathogenic agents and are supervised by scientists competent in handling infectious agents and associated procedures; 2) access to the laboratory is restricted when work is being conducted; and 3) all procedures in which infectious aerosols or splashes may be created are conducted in BSCs or other physical containment equipment such as centrifuge safety cups and sealed rotors.

The following standard and special practices, safety equipment, and facility requirements apply to BSL-2:

Standard Microbiological Practices

- The laboratory supervisor enforces the institutional policies that control safety in and access to the laboratory.
- The laboratory supervisor ensures that laboratory personnel receive appropriate training regarding their duties, potential hazards, manipulations of infectious agents, necessary precautions to minimize exposures, and hazard/exposure evaluation procedures (e.g., physical hazards, splashes, aerosolization) and that appropriate records are maintained. Personnel receive annual updates and additional training when equipment, procedures, or policies change. All persons entering the facility are advised of the potential hazards, are instructed on the appropriate safeguards, and read and follow instructions on practices and procedures. An institutional policy regarding visitor training, occupational health requirements, and safety communication is considered.
- Personal health status may affect an individual's susceptibility to infection and ability to receive available immunizations or prophylactic interventions. Therefore, all personnel, and particularly those of reproductive age and/or those having conditions that may predispose them to increased risk for infection (e.g., organ transplant, medical immunosuppressive agents), are provided information regarding immune competence

and susceptibility to infectious agents. Individuals having such conditions are encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance.

- A safety manual specific to the facility is prepared or adopted in consultation with the facility director and appropriate safety professionals. The safety manual is available, accessible, and periodically reviewed and updated as necessary.
    - The safety manual contains sufficient information to describe the biosafety and containment procedures for the organisms and biological materials in use, appropriate agent-specific decontamination methods, and the work performed.
    - The safety manual contains or references protocols for emergency situations, including exposures, medical emergencies, facility malfunctions, and other potential emergencies. Training in emergency response procedures is provided to emergency response personnel and other responsible staff according to institutional policies.
- A sign incorporating the universal biohazard symbol is posted at the entrance to the laboratory when infectious materials are present. Posted information includes: the laboratory's Biosafety Level, the supervisor's or other responsible personnel's name and telephone number, PPE requirements, general occupational health requirements (e.g., immunizations, respiratory protection), and required procedures for entering and exiting the laboratory. Agent information is posted in accordance with the institutional policy.
- Long hair is restrained so that it cannot contact hands, specimens, containers, or equipment.
- Gloves are worn to protect hands from exposure to hazardous materials.
    - Glove selection is based on an appropriate risk assessment.
    - Gloves are not worn outside the laboratory.
    - Change gloves when contaminated, glove integrity is compromised, or when otherwise necessary.
    - Do not wash or reuse disposable gloves, and dispose of used gloves with other contaminated laboratory waste.
- Gloves and other PPE are removed in a manner that minimizes personal contamination and transfer of infectious materials outside of the areas where infectious materials and/or animals are housed or manipulated.
- Persons wash their hands after working with potentially hazardous materials and before leaving the laboratory.
- Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption are not permitted in laboratory areas. Food is stored outside the laboratory area.
- Mouth pipetting is prohibited. Mechanical pipetting devices are used.

- Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassware are developed, implemented, and followed; policies are consistent with applicable state, federal, and local requirements. Whenever practical, laboratory supervisors adopt improved engineering and work practice controls that reduce risk of sharps injuries. Precautions are always taken with sharp items. These include:
    - Plasticware is substituted for glassware whenever possible.
    - Use of needles and syringes or other sharp instruments is limited in the laboratory and is restricted to situations where there is no alternative (e.g., parenteral injection, blood collection, or aspiration of fluids from laboratory animals or diaphragm bottles). Active or passive needle-based safety devices are to be used whenever possible.
        - Uncapping of needles is performed in such a manner to reduce the potential for recoil causing an accidental needlestick.
        - Needles are not bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal.
        - If absolutely necessary to remove a needle from a syringe (e.g., to prevent lysing blood cells) or recap a needle (e.g., loading syringes in one room and injecting animals in another), a hands-free device or comparable safety procedure must be used (e.g., a needle remover on a sharps container, the use of forceps to hold the cap when recapping a needle).
        - Used, disposable needles and syringes are carefully placed in puncture-resistant containers used for sharps disposal immediately after use. The sharps disposal container is located as close to the point of use as possible.
    - Non-disposable sharps are placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving.
    - Broken glassware is not handled directly. Instead, it is removed using a brush and dustpan, tongs, or forceps.
- Perform all procedures to minimize the creation of splashes and/or aerosols.
- Decontaminate work surfaces after completion of work and after any spill or splash of potentially infectious material with appropriate disinfectant. Spills involving infectious materials are contained, decontaminated, and cleaned up by staff who are properly trained and equipped to work with infectious material. A spill procedure is developed and posted within the laboratory.
- Decontaminate all cultures, stocks, and other potentially infectious materials before disposal using an effective method, consistent with applicable institutional, local, and state requirements. Depending on where the decontamination will be performed, the following methods are used prior to transport:
    - Materials to be decontaminated outside of the immediate laboratory are placed in a durable, leak-proof container and secured for transport. For infectious

materials, the outer surface of the container is disinfected prior to moving materials and the transport container has a universal biohazard label.

- Materials to be removed from the facility for decontamination are packed in accordance with applicable local, state, and federal regulations.

- An effective integrated pest management program is implemented.
- Animals and plants not associated with the work being performed are not permitted in the laboratory.

Special Practices

- Access to the laboratory is controlled when work is being conducted.
- The laboratory supervisor is responsible for ensuring that laboratory personnel demonstrate proficiency in standard microbiological practices and techniques for working with agents requiring BSL-2 containment.
- Laboratory personnel are provided medical surveillance, as appropriate, and offered available immunizations for agents handled or potentially present in the laboratory.
- Properly maintained BSCs or other physical containment devices are used, when possible, whenever:
    - Procedures with a potential for creating infectious aerosols or splashes are conducted. These include pipetting, centrifuging, grinding, blending, shaking, mixing, sonicating, opening containers of infectious materials, inoculating animals intranasally, and harvesting infected tissues from animals or eggs.
    - High concentrations or large volumes of infectious agents are used. Such materials may be centrifuged in the open laboratory using sealed rotors or centrifuge safety cups with loading and unloading of the rotors and centrifuge safety cups in the BSC or another containment device.
    - If it is not possible to perform a procedure within a BSC or other physical containment device, a combination of appropriate personal protective equipment and administrative controls are used, based on a risk assessment.
- Laboratory equipment is decontaminated routinely; after spills, splashes, or other potential contamination; and before repair, maintenance, or removal from the laboratory.
- A method for decontaminating all laboratory waste is available (e.g., autoclave, chemical disinfection, incineration, or other validated decontamination method).
- Incidents that may result in exposure to infectious materials are immediately evaluated per institutional policies. All such incidents are reported to the laboratory supervisor and any other personnel designated by the institution. Appropriate records are maintained.

Safety Equipment (Primary Barriers and Personal Protective Equipment)

- Protective laboratory coats, gowns, or uniforms designated for laboratory use are worn while working with hazardous materials and removed before leaving for non-laboratory areas (e.g., cafeteria, library, and administrative offices). Protective clothing is disposed

of appropriately or deposited for laundering by the institution. Laboratory clothing is not taken home.

- Eye protection and face protection (e.g., safety glasses, goggles, mask, face shield or other splatter guard) are used for manipulations or activities that may result in splashes or sprays of infectious or other hazardous materials. Eye protection and face protection are disposed of with other contaminated laboratory waste or decontaminated after use.
- The risk assessment considers whether respiratory protection is needed for the work with hazardous materials. If needed, relevant staff are enrolled in a properly constituted respiratory protection program.
- In circumstances where research animals are present in the laboratory, the risk assessment considers appropriate eye, face, and respiratory protection, as well as potential animal allergens.

Laboratory Facilities (Secondary Barriers)

- Laboratory doors are self-closing and have locks in accordance with the institutional policies.
- Laboratories have a sink for handwashing. It should be located near the exit door.
- An eyewash station is readily available in the laboratory.
- The laboratory is designed so that it can be easily cleaned.
    - Carpets and rugs in laboratories are not appropriate.
    - Spaces between benches, cabinets, and equipment are accessible for cleaning.
- Laboratory furniture can support anticipated loads and uses.
    - Benchtops are impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals.
    - Chairs used in laboratory work are covered with a non-porous material that can be easily cleaned and decontaminated with appropriate disinfectant.
- Laboratory windows that open to the exterior are not recommended. However, if a laboratory does have windows that open to the exterior, they are fitted with screens.
- Illumination is adequate for all activities and avoids reflections and glare that could impede vision.
- Vacuum lines in use are protected with liquid disinfectant traps and in-line HEPA filters or their equivalent. Filters are replaced, as needed, or are on a replacement schedule determined by a risk assessment.
- There are no specific requirements for ventilation systems. However, the planning of new facilities considers mechanical ventilation systems that provide an inward flow of air without recirculation to spaces outside of the laboratory.
- BSCs and other primary containment barrier systems are installed and operated in a manner to ensure their effectiveness.

- BSCs are installed so that fluctuations of the room air supply and exhaust do not interfere with proper operations. BSCs are located away from doors, windows that can be opened, heavily traveled laboratory areas, and other possible airflow disruptions.
- BSCs can be connected to the laboratory exhaust system by either a canopy connection (Class IIA only) or directly exhausted to the outside through a hard connection (Class IIB, IIC, or III). Class IIA or IIC BSC exhaust can be safely recirculated back into the laboratory environment if no volatile toxic chemicals are used in the cabinet.
- BSCs are certified at least annually to ensure correct performance.

BSL-2 Enhanced (BSL-2+)

This level is not described in the BMBL but is often used as a hybrid safety level between BSL-2 and BSL-3. With this level, there is work done with materials that may be infectious primarily via an aerosol and introduction through the skin or mucous membranes. Risk is elevated above basic BSL-2 due to the insert location, vector, or cell line. At this level, risk can be controlled by adherence to some BSL-3 practices and PPE within a physical BSL-2 laboratory. Specific laboratory practices and experimental procedures must be outlined in a working protocol for the laboratory as the result of a specific Risk Analysis.

Biosafety Level 3 (BSL-3)

This level identifies an inhalation exposure risk. Risk group 3 agents which are highly infectious and for which treatment may not be available are used. As examples, tuberculosis and anthrax are used in BSL-3 containment. Work at BSL-3 is allowed in some cities under separate permit from the municipal regulatory bodies. A secure and controlled laboratory environment is required. See the BMBL for specific physical laboratory requirements and practices. Work at BSL-3 is prohibited at AbCellera Boston.

Biosafety Level 4 (BSL-4)

This is the highest containment level as described by the CDC/NIH. Risk Group 4 agents which are extremely infectious are used at BSL-4 containment; examples are Ebola and Variola virus. BSL-4 work is prohibited in most cities. See the BMBL for specific physical laboratory requirements and practices. Work at BSL-4 is prohibited in the Town of Arlington.

5.

HUMAN MATERIALS AND OTHER POTENTIALLY INFECTIOUS MATERIALS (OPIM)

The OSHA Bloodborne Pathogens Standard defines safety requirements for working with human blood and other clinical materials, human immunodeficiency virus, and the bloodborne hepatitis viruses. Those safety requirements are described in this Biosafety Manual and Exposure Control Plan. Before working with any human materials, contact the Biosafety Officer for guidance and to schedule Bloodborne Pathogens training.

The Standard establishes the principle that blood and certain body fluids of all human beings are considered potentially infectious for bloodborne pathogens such as hepatitis B or C virus (HBV, HCV) and human immunodeficiency virus (HIV).

It further establishes that universal precautions are to be used to prevent parenteral, mucous membrane, and non-intact skin exposure to bloodborne pathogens when handling human blood, human blood components, products made from human blood and other potentially infectious materials (OPIM). Refer to Appendix I for the list of OPIM that fall under the OSHA Standard.

Universal precautions do not apply to the following human materials unless visibly contaminated with blood: urine, feces, sputum, saliva, tears, sweat, nasal secretions, vomitus.

While these materials are not covered by the Bloodborne Pathogens Standard, they may be contaminated with infectious microorganisms and can present a potential hazard to persons working with them. Prudent handling practices are recommended for work with any human material.

Materials other than those mentioned above which should also be handled at BSL-2 containment using universal precautions are human derived cell lines, human cell strains, and human serum derived reagents.

Human Cell Lines

Characterization of human cells, for inclusion or exclusion from compliance with the Bloodborne Pathogens Standard, would include screening of the cells lines for viruses characterized as bloodborne pathogens by the Standard, including human immunodeficiency viruses, hepatitis viruses and EBV, if the cells are capable of propagating such viruses. Testing may include antigenic screening for viral or agent markers, co-cultivation with various indicator cells that allow contaminants to grow, or using molecular technology such as polymerase chain reaction or nucleic acid hybridization, to identify latent viruses capable of infecting humans. These are viruses such as Herpesviruses like Epstein Barr Virus, or papilloma members of the Papovavirus group. Cell lines that are procured from commercial vendors or other sources with documented testing to be free of human bloodborne pathogens and which have been protected by the employer from environmental contamination may be excluded from the Bloodborne Pathogens Standard.

It should be noted that human cells or other transformed human cell lines are sometimes adulterated with laboratory pathogens accidentally introduced by cultivation with other cell cultures, or physically contaminated by other cell cultures handled in the same laboratory. To handle human cells, without having to comply with the requirements of the Bloodborne Pathogens Standard, human cells should be documented to be pure cells and shown to be free

of Bloodborne Pathogens by testing as explained above. Even common cell lines, such as human cervical carcinoma cells, known as HeLa cells, would need documentation on purity prior to downgrading. Please note that if a cell line is proven to be BBP free, it may be removed from the requirements of the Bloodborne Pathogens Standard, but a full risk assessment would be required to also downgrade the material to BSL-1.

Human Cell Strains

All primary human cell **explants** from tissues and **subsequent in vitro** passages of human tissue explant cultures, also known as human cell strains, must be regarded as containing potential bloodborne pathogens and should be handled in accordance with the Bloodborne Pathogens Standard. Non-transformed, human cell strains, characterized by documented, reasonable laboratory testing as described for human cell lines, to be free of human immunodeficiency virus, hepatitis viruses, or other bloodborne pathogens may be exempted from the standard's requirements. However, if such tissue explants or subsequent cultures are derived from human subjects known to carry bloodborne pathogens, such as hepatitis viruses or human immunodeficiency viruses or are deliberately infected with bloodborne pathogens, they must be handled in accordance with the precautions noted in the Bloodborne Pathogens Standard. Likewise, animal tissues, explants or cell cultures known to be contaminated by deliberate infection with human immunodeficiency virus or Hepatitis B virus are also subject to the Standard.

Human Derived Reagents

The Centers for Disease Control and Prevention cautions that all human-serum-derived reagents used in the lab, such as Human Serum Albumin (HSA), be handled at BSL-2 levels with universal precautions because no test method can offer complete assurance that laboratory specimens do not contain HIV, hepatitis B virus, or other infectious agents.

Non-Human Primate (NHP) Material

The close genetic relationship between humans and Non-Human Primates (NHP) may lead to a greater occurrence of zoonosis. Because of this, all work with NHP tissues and cells must be handled at BSL-2.

NHP material from Macaques may be contaminated with *Macacine alphaherpesvirus 1* (McHV-1), also called B virus or Herpes B Virus. McHV-1 is the only identified nonhuman primate herpesvirus that displays severe pathogenicity in humans. This zoonotic disease causes severe central nervous system disease and is potentially fatal in humans. It may be present in asymptomatic animals, and positive animals often do not present with circulating antibodies. For these reasons, all NHP material are handled at BSL-2 at a minimum. Saliva, feces, urine, tissues, and cells lines primarily from brain and spinal cord can be a source of exposure to the virus. Work with NHP material that is known to contain McHV-1 must undergo a full risk assessment and may be handled at a higher biosafety level or with enhanced practices.

For any exposure to NHP material, clean the area and seek medical advice immediately.

6. RECOMBINANT AND SYNTHETIC NUCLEIC ACID MOLECULES

Research with recombinant or synthetic nucleic acid molecules (e.g., rDNA) is regulated typically by two organizations: the National Institutes of Health (NIH) and the local public health department. For facilities receiving federal funds for recombinant or synthetic nucleic acids research, adherence to the NIH Guidelines is mandatory, even for projects at the same facility which are not funded by the NIH. For facilities that do not receive federal funding, the local public health department is the primary regulatory agency. Each local public health department may have its own ordinance which requires a facility to abide by the NIH Guidelines in total, or in part.

A copy of the NIH Guidelines can be found online at https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf. The Biosafety and Recombinant DNA Regulations for the Town of Arlington can be found in Appendix IV.

NIH Guideline Requirements

Establish an Institutional Biosafety Committee (IBC)

AbCellera Boston has established an IBC and procedures that the IBC will follow in its review of project registration proposals and activities. Formal minutes of the IBC meetings are written and kept on file at the institution. These minutes will not contain proprietary company information and therefore will be made available to the public as requested. The Town of Arlington requires that IBC minutes be submitted to the Board of Health Director by April 30 of each year as part of the annual report.

An IBC is comprised of no fewer than five members with collective expertise and experience with recombinant or synthetic nucleic acids technology, the ability to assess safety and identify potential risk to workers and the environment, and expertise in physical containment. At least one member of the committee must be from the laboratory technical staff (non-Ph.D. level scientist). One member can be a consultant knowledgeable in institutional policies, applicable law, and the environment. Membership must also include:

- At least two members not associated with the institution who act as “Community Representatives”; at least one member will be an Arlington resident approved by the Board of Health
- An expert in plants, plant pathogens and plant pest containment principles when plants are proposed for use in the registration
- An expert in animal containment principles when animals are proposed for use in the registration
- The Biological Safety Officer as best practice
- Participants with adequate expertise and training if human subjects are involved

The IBC reviews and assesses all registrations for safety and ensures that all projects conform with the Guidelines. The initial and periodic review includes an assessment of the appropriate containment level required by the Guidelines for the proposed research and an assessment of the facilities, procedures, practices, training and expertise of personnel working with recombinant or synthetic nucleic acid molecules, and recommends emergency plans and appropriate medical surveillance for the personnel as necessary.

Project Registrations

All Principal Investigators planning to work with recombinant or synthetic nucleic acid molecules must complete a Project Registration document prior to beginning work. If BSL-2 or BSL-2 Enhanced containment is necessary for a project, the registration must be approved by the Institutional Biosafety Committee prior to initiation. Work with nucleic acid primers and oligonucleotides is not subject to the NIH Guidelines. The project registration form is given in Appendix V.

Training for Employees

All employees involved in recombinant or synthetic nucleic acid molecules research are given biological safety training. In addition, project specific training will be provided by the Principal Investigator of the project before initiating work.

Medical Surveillance

Medical surveillance for each project will be decided upon by the IBC. Project specific medical surveillance programs will be included on the registration document.

Accident/Incident Reports

Any accidents, illnesses, releases, or significant problems that occur while working with recombinant or synthetic nucleic acid molecules will be reported to NIH Office of Science Policy (OSP). At the local level, any accidental release or exposure to recombinant or synthetic nucleic acid molecules, which represents a significant potential hazard to employees or the public or any significant biological agent-related accident or illness shall also be reported to the Arlington Board of Health immediately and in no case more than twenty-four hours after the release, exposure, accident or illness. The initial report shall be provided verbally, with a written report documenting the initial report to follow within 24 hours. A final written report shall be provided to the Arlington Board of Health within 30 days of the initial report.

Retroviruses

Retroviral vectors are a common tool used in cell biology. Retroviruses package RNA molecules into virus particles and express a messenger RNA of interest. The retroviral genome expressed in packaging cell lines is not intact, therefore no replication competent virus (RCV) is produced. Because of this, virus particles are “infectious” for only one replication cycle. However, the possibility exists for recombination with endogenous retroviral elements, or with an exogenous retroviral infection, such as HIV. This is the primary risk when using retroviral vectors.

Another risk involved with retroviral vectors is the target cell range of the vector. For example: if RNA is packaged in particles with the envelope protein of vesicular stomatitis virus (VSV-G

protein) this provides a broad target cell range because most cell types express the phospholipids to which VSV-G protein binds. Appendix VI describes retroviral vectors in more detail.

Adeno-Associated Virus (AAV)

Adeno-associated virus (AAV) and recombinant adeno-associated virus (rAAV) are commonly used in gene expression experiments. These viral vectors are sometimes preferred because they are primarily episomal, and less of a biosafety concern compared to lentiviral vectors, which can integrate into the host genome. Appendix VII provides more information about AAV.

7.

SELECT AGENTS

The Centers for Disease Control and Prevention (CDC) regulation “Requirements for Facilities Transferring or Receiving Select Agents” (42 CFR 72.6) was developed in response to The United States Antiterrorism and Effective Death Penalty Act. The CDC regulation was implemented to reduce the risk that terrorists or others with illicit intentions would gain access to and misuse such materials. It addresses the domestic shipment and handling of certain infectious agents and toxins. The CDC list of select agents that cause substantial harm to human health can be found in Appendix VIII of this manual.

A permit must be obtained from the CDC before select agents or toxins above the permissible toxin amounts may be shipped or received. To obtain a permit for Select Agents, the facility must be registered and create a Select Agents program.

This manual does not cover a Select Agents program. For more details on Select Agents programs, see the Federal Select Agents Program website at http://www.selectagents.gov/.

8. EXPOSURE DETERMINATION

The OSHA Bloodborne Pathogens Standard requires that an exposure determination be performed in laboratories where human source materials are used. A list of departments, job classifications, tasks, and responsibilities must be made to identify all employees that may have exposure to human materials.

Job Classifications

Employees of the following departments may have exposure to human source materials:

- Genetics
- Immunology
- Molecular Biology

The potential for occupational exposure to human blood and other potentially infectious materials may occur with these job classifications:

- Research Associate
- Research Scientist I
- Research Scientist II
- Head of Genetics
- Associate Director
- Senior Vice President of Research

Tasks and Procedures

The following tasks or procedures may cause potential exposures to personnel listed in the above job classifications:

- Work with human cell lines
- Shipping or receiving human source materials
- Closing up, boxing or moving biomedical waste containers

9.

ENGINEERING CONTROLS

Engineering and work practice control measures are to be used to minimize, isolate, or eliminate employee exposure for each task within the work area. Such control measures are listed below.

Engineering controls must be the primary means of eliminating or minimizing employee exposure and include the use of safer medical devices (safer sharps), such as needleless devices, shielded needle devices, plastic capillary tubes and retractable scalpel/knife blades.

Engineering controls are used when there is reasonable likelihood of occupational exposure. Engineering controls are examined, and maintained or replaced, on a regular schedule by the supervisor and employee to ensure their effectiveness. Current regulations state that "safer medical devices, such as sharps with engineered sharps injury protections and needleless systems" constitute engineering controls and thus must be used where feasible. Individuals using these devices should have input into their selection.

It is important to note that each laboratory employee is responsible for reviewing the effectiveness of the engineering controls before use. When occupational exposure remains after institution of these controls, personal protective equipment (PPE) is used. PPE is discussed in section 10, “Work Practices”.

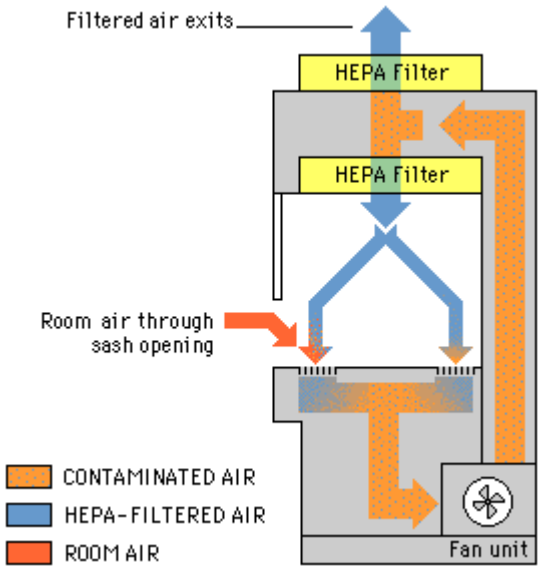
Biosafety Cabinet (BSC)

Biosafety cabinets are the primary control against potential aerosol exposure. They are designed to provide protection for both the worker, the work, as well as provide a work environment free of contaminants. There are many types of BSCs available which offer various levels of protection. Information about the variety of types of biosafety cabinets can be found in appendix A of the BMBL.

Requirements for Class II biosafety cabinets in the United States are established by NSF International and published in NSF/ANSI Standard 49. NSF 49 includes definitions of the types and function, acceptable materials, design and construction requirements, and performance requirements for Class II biological safety cabinets.

Protection offered by BSCs is a factor of three separate directional airflows:

- Inward airflow from the room through the front grille provides personal protection
- Downward airflow through a HEPA filter onto the work surface provides product protection
- Airflow out of the cabinet through an exhaust HEPA filter provides environmental protection



Air Flow

HEPA filters protect against particulates. BSCs have a digital or analog gauge that monitors the performance of the filter. Biosafety cabinets must be calibrated, and the gauge must read steady at the level indicated by the certification sticker affixed to the BSC. If the reading falls below the certification level indicated, do not use the BSC and notify the Project Manager so the filter can be replaced.

If the BSC alarm goes off, cap any tubes quickly and close the sash. Contact the Project Manager/Biosafety Officer for evaluation. Post the door of the laboratory with a “Do Not Enter” sign.

Using the BSC

The effectiveness of the biosafety cabinet is directly dependent on the way users perform their work. Examine and disinfect the BSC after each scientific procedure and check the functionality of the HEPA filter each time the BSC is used.

- It is good microbiological practice to wipe down the cabinet work surface with disinfectant before beginning work.
- Supplies needed for work should be placed into the cabinet. If the blower is off, turn the blower on and allow the cabinet to run for 10-15 minutes before beginning work to establish proper airflow.
- The vertical sash is kept below the indicated calibrated height.
- Avoid creating turbulence in the cabinet by only placing those supplies needed for the experiment into the cabinet. Movement in and out of the cabinet should be deliberate and perpendicular to the front grille.
- The work area should be set up with a workflow pattern of clean to dirty.
- All air grates are kept clear, including the front and sides.
- When work is finished, wipe down all surfaces with disinfectant.
- If the BSC is not being used, keep the vertical sash down and shut the blower off.
- Most biosafety cabinets use recirculated airflow; therefore, hazardous chemicals cannot be used within them.
    - A hard-ducted biosafety cabinet may be appropriate for hazardous chemical use, however spark potential from the motor is still a concern for use with flammable material.
    - All BSCs at AbCellera Boston use recirculated air; no cabinets are hard ducted to roof exhaust. Therefore, use of hazardous chemicals is prohibited within the cabinet. Motors and lights are not explosion proof, so flammables should not be used.

Turbulence in the BSC

Turbulence may cause aerosols which can cross-contaminate open vessels or escape the cabinet and potentially cause exposure. Turbulence can be caused by various factors:

- Blocking air flow grilles
- Air current eddies caused by heat from Bunsen burners or other heat sources (Bunsen burners should not be used in a BSC)
- Rapid movement of arms into or out of the cabinet
- Rapid movement behind the worker and across the face of the cabinet
- Down drafts from ventilation systems. BSCs should be located in areas away from ventilation intakes for this reason.
- Cross drafts from opening doors near the BSC

Other BSC Considerations

- Do not store anything on top of the biosafety cabinet
- Affix a biohazard warning label on each BSC
- BSCs should be located several feet from doors. If possible, they should be spaced at least 6 feet apart and not directly across from another BSC.

BSC Certification

Biosafety cabinet field tests should be performed by the certifier upon installation and relocation of cabinets, after major maintenance or changing of HEPA filters is conducted, and at regular intervals thereafter. NSF 49 recommends no more than 12 months between certifications. The field tests are related to the containment and product protection provided by the cabinet, and results must correlate to the value obtained by NSF for type testing of the make, model, and size of cabinet (the certification values should be provided by the cabinet's manufacturer). Certification should cover the following:

- Downflow velocity test
- Inflow velocity test
- Airflow smoke pattern tests
- HEPA filter leak test
- Cabinet integrity test (for Type A1 cabinets with positive-pressure contaminated plenums only)
- Alarm function verification
- Blower interlock (for Type B1 and B2 cabinets)
- Exhaust system performance (for any cabinet connected to the building exhaust system)

Sharps Containers

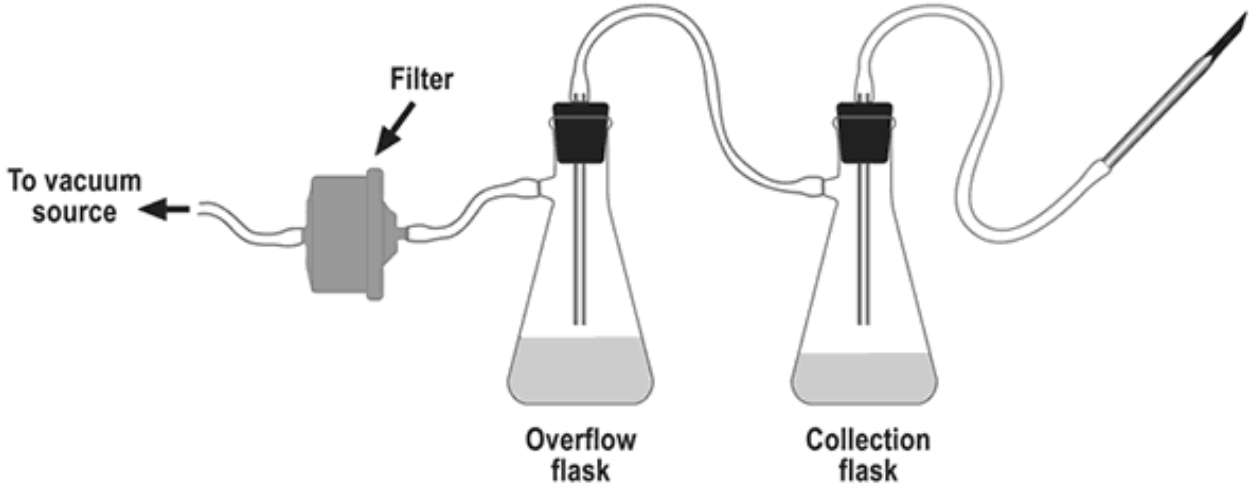
Sharps containers are made of puncture resistant material, typically polypropylene or plastic. Containers are examined and maintained after each procedure to ensure they are not compromised. When a container is full it is sealed and brought to the waste storage room by the Biosafety Officer. A new container is then put into service.

Aspiration Filters

Aspiration units used with Risk Group 2 or higher materials must be fitted with an in-line HEPA/hydrophobic filter. This filter protects the house vacuum system, or pump, from potential contamination. Check the filter before each procedure to ensure there is no liquid contamination.

Aspiration Guidelines

Protecting the vacuum line is one of the goals of proper aspiration set-up. The Vacushield™ or other in-line filter, reduces risk of contaminating the in-house vacuum. The second line of defense is the overflow flask which is set up behind the primary collection flask. See the figure below for proper set-up, showing locations of the primary collection flask, the overflow flask, and the in-line filter.



Aspiration Work Practices

Always pre-measure disinfectant and add it to the collection flask before beginning work so that waste is disinfected as it is collected. Label the flask accordingly with biohazard waste and disinfectant name. Change the disinfectant daily, as appropriate.

If the collection and overflow flasks are on the floor, protect against breakage and use secondary containment to catch any spills.

When removing the stopper from the collection flask, work in the biosafety cabinet to prevent exposure from aerosols generated by splatter or splash.

Plexiglass Shielding

Plexi shielding, either in the form of a bench shield or a faceshield, is used to provide protection from splash or splatter when working with materials outside of a BSC. Biohazardous work done on a bench instead of in a BSC must be reviewed and assessed by the Biosafety Officer prior to the initiation of work.

Examine and disinfect plexi shields after each procedure.

10. WORK PRACTICES

Universal Precautions

When human source materials are used, universal precautions must be adhered to. “Universal precautions” means treating material as if it is known to be infectious. When using universal precautions, one performs tasks using practices to prevent contact with blood or other potentially infectious materials. When differentiation between body fluid types is difficult or impossible, all body fluids are considered potentially infectious materials.

Minimum Requirements for Work in a Biological Lab

- Wash hands immediately, or as soon as feasible, after removal of gloves or other personal protective equipment. Each laboratory has hand washing sinks.
- Following contact with blood or other potentially infectious materials, wash hands and any other affected skin with soap and water
- Do not bend, shear, or break needles and other sharps
- Do not recap needles. If recapping is absolutely necessary, perform a risk assessment, and use single handed recapping devices.
- Never remove a needle from a syringe; dispose as a unit
- Immediately, or as soon as possible after use, place contaminated sharps in puncture-resistant, labeled, leakproof containers. Sharps containers are located at each employee’s laboratory bench. Close full sharps containers and move to the biowaste room. Medical/biohazardous waste is shipped out for processing by a licensed medical waste transporter. AbCellera Boston’s medical waste transporter is Veolia Environmental Services.
- Food and drink are prohibited from laboratory space and work areas including refrigerators, freezers, shelves, cabinets, countertops, and benchtops. Laboratory space includes the laboratories themselves and the laboratory hallways.
- Smoking, applying cosmetics, and handling contact lenses are prohibited in all laboratory work areas
- Avoid hand contact with your mouth, nose, and eyes
- Protect wounds and dermatitis with bandages and gloves, and double glove
- Perform all procedures involving blood, or other potentially infectious materials in a manner that minimizes splashing, spraying, spattering, and generation of droplets of these substances. The following procedures have this potential and methods which will minimize these risks are provided:

  - Transfer liquid samples between containers in the biological safety cabinet or behind a benchtop safety shield
  - Centrifuge liquid samples in tightly closed bottles, within covered centrifuge rotors, within covered centrifuges. Allow to settle for 10 minutes prior to opening on the bench or open in a biological safety cabinet.
  - Concentrate liquid samples under nitrogen pressure behind benchtop safety shields. Cover the pressure release valve with absorbent materials during pressure release.
  - When vortexing liquid samples, use test tube caps to cover samples. Place gauze around cap before opening.
  - When aspirating liquid samples, use an overflow flask and an in-line HEPA/hydrophobic filter for protection of vacuum lines. Remove stopper from waste flask in the biosafety cabinet.

- Mouth pipetting is prohibited
- Place specimens of blood or other potentially infectious materials in a container that prevents leakage during collection, handling, processing, storage, or transport. Close the container prior to storing or transporting. Label specimens with the Universal Biohazard Symbol prior to transport from one location to another, both within and outside the facility.
- If outside contamination of the primary container occurs, place the primary container within a secondary container that prevents leakage. If a specimen could puncture the primary container, place the primary container within a secondary puncture-resistant container. Secondary containers in the laboratory areas include closable, leakproof plasticware such as Tupperware™ or Rubbermaid® containers.
- Examine all equipment which may become contaminated with blood or other potentially infectious materials prior to servicing or shipping. Decontaminate, as necessary, using standard disinfection methods. If decontamination of the equipment or portions of such equipment is not feasible, attach a readily observable label with the Universal Biohazard Symbol to the equipment stating which portions remain contaminated. Convey this information to all affected employees, the servicing representative, and/or the manufacturer as appropriate prior to handling, servicing, or shipping so that the appropriate precautions are taken.
- Avoid the use of sharps in the laboratory whenever possible. Double edged razors are forbidden in the laboratory. Sheaths must be used to cover razors or scalpels when not in use. Use box cutters for opening packages and for cutting, when possible. Never recap, bend, shear, or break needles. Use Luer-Lock fittings for all needleless systems, syringes, needles, or use integrated needle-syringe units. Dispose of all needles/syringes as a unit; do not remove the needle from a syringe before disposal. Dispose of ALL sharps into a puncture resistant sharps container. Any sharps work with materials needing BSL-2 containment entails prior notification to the Biosafety Officer and documented training.
- Substitute plastic for glass whenever possible in the laboratory. This reduces the sharps exposure risk.

Personal Protective Equipment (PPE)

Personal protective equipment is provided by the company at no cost to the employee when there is potential for occupational exposure to biohazards. Appropriate personal protective equipment may consist of, but is not limited to, gloves, lab coats, gowns, eye protection, masks and faceshields. All personal protective equipment must be readily accessible and available in the appropriate sizes.

Personal protective equipment is available throughout the laboratories and obtained by the employee as needed. The Project Manager/Biosafety Officer will ensure that the necessary equipment and clothing are available in these locations.

It is the employee's responsibility when there is occupational exposure, or the potential for exposure, to use the appropriate personal protective equipment and clothing.

PPE Guidelines

PPE guidelines apply to all labs, glasswash, and media prep areas.

- Open toed shoes or sandals are not allowed in the laboratory areas. Footwear worn in the laboratory must cover the entire foot. Mesh-topped shoes, such as athletic shoes, should be avoided.
- Personal attire that does not cover the entire leg is not allowed in the laboratory.
- Only low allergen, non-powdered, non-latex gloves are used in the laboratories.
- Protective eyewear will be worn in all laboratories and in the laboratory hallways.
- PPE must not be worn out of the laboratory areas except when transporting lab materials between laboratories. Office areas and carpeted areas throughout the building are strictly off limits for PPE.
- Unless the door handles are clearly labeled for glove use, **never touch doorknobs with gloves, even if they are clean!** This will lessen the chance of the spread of contamination.
- If transporting laboratory material on a cart, do not touch the cart handle with gloves. Keep spare gloves on the cart to use when touching the laboratory material.

PPE Requirements

Biosafety Level	Required PPE	Recommended PPE
BSL-1	Safety glasses, buttoned lab coats, gloves; face shields for cryogenic work	Face shields and goggles when splashes or splatters can occur
BSL-2	Safety glasses, buttoned lab coats, gloves; face shields for cryogenic work	Face shields and goggles when splashes or splatters can occur

Remove contaminated personal protective garments immediately, or as soon as feasible, and prior to leaving the work area. Place non-disposable lab coats which are visibly contaminated in the biohazard waste container. Remove unsoiled lab coats and leave in the designated area for reuse prior to leaving the area. Lab coats that are offered for pick-up are laundered and returned the following week. Place disposable lab coats in a biohazardous waste container.

Wear gloves when hand contact with blood, other potentially infectious materials, mucous membranes, and non-intact skin can be reasonably anticipated, and when handling or touching contaminated items or surfaces. Wear gloves for all procedures involving blood, samples derived from blood, and other human materials. Wear gloves of the appropriate type when working with chemicals.

Replace disposable gloves as soon as practical when contaminated; or as soon as feasible if they are torn, punctured, or when their ability to function as a barrier is compromised. Dispose of gloves in the biohazard waste containers located in the laboratory areas. Gloves, even when clean, should not be placed in regular trash. Remove and dispose of gloves before leaving the work area.

Do not wash or decontaminate disposable gloves for reuse. Utility gloves (e.g., rubber household gloves) may be used for housekeeping chores involving potential blood contact and for instrument cleaning and decontamination procedures. Utility gloves may be decontaminated and re-used, but should be discarded if they are peeling, cracked, or discolored, if they have punctures or other evidence of deterioration, or if their ability to function as a barrier is compromised.

Safety glasses are required of all personnel in all laboratory areas. Use a chin-length face shield whenever splashes, spray, splatter, aerosols or droplets of blood or other potentially infectious materials may be generated, and eye, nose, or mouth contamination can be reasonably anticipated. The IBC/Safety Committee must evaluate situations that may require goggles in addition to a full faceshield when such operations cannot be performed behind a suitable shield or in a biosafety cabinet. Disinfect or dispose of faceshields in the biohazard waste container when contaminated. Non-contaminated face shields remain in the work area for future use.

Housekeeping

The worksite is maintained in a clean and sanitary condition according to a written schedule for cleaning and use of the proper methods of decontamination. The schedule and methods are based upon the location of the worksite within the facility, the type of surface to be cleaned, the type of soil present, and the tasks or procedures being performed in that area. The written schedule is in Appendix IX.

Clean and decontaminate equipment and working surfaces after contact with blood or other potentially infectious materials with an appropriate disinfectant:

- After completion of procedures
- Immediately or as soon as feasible when surfaces are overtly contaminated
- After any spill of blood or other potentially infectious materials
- At the end of the workday

Remove and replace protective coverings on equipment and surfaces as soon as feasible when they become contaminated. Bench paper with impermeable plastic backing or washable trays may be used to protect benchtop surfaces from contamination. If bench paper is used, once the paper is contaminated disposed of this in the biohazard waste container. It is recommended to use bench coverings as little as possible to promote cleaning and disinfection. Coverings should not be placed under equipment that is not easy to move for cleaning. Replace coverings on an as-needed basis or per the schedule in Appendix IX.

Inspect and decontaminate all reusable bins, pails, cans and similar receptacles which have a reasonable likelihood of becoming contaminated with blood or other potentially infectious materials on a regular basis. Clean and decontaminate these immediately, or as soon as feasible, upon visible contamination. Monitor all biohazardous waste containers at least weekly. If contaminated or found to be leaking, decontaminate and replace if necessary.

Disposal of all regulated waste is in accordance with the Massachusetts Sanitary Code (105 CMR 480.000) and the waste disposal policies of AbCellera Boston.

Ancillary staff who enter the laboratories for housekeeping must follow the requirements in Appendix X.

Safer Sharps

AbCellera Boston has instituted a safer sharps program in compliance with the OSHA Bloodborne Pathogens Standard for all employees that use sharps with human materials or OPIM. Since no one device will be appropriate or effective for all circumstances, employers must select devices that are based on reasonable judgment, such as

- The sharp will not jeopardize employee safety or be medically inadvisable
- The sharp will make an exposure incident involving a contaminated sharp less likely to occur

Employers must solicit input from those non-managerial employees responsible for the use of engineered controls regarding the identification, evaluation, and selection of those controls, including safer medical devices. The sharps evaluation form is in Appendix XI. The employees selected should represent the range of exposure situations encountered in the workplace, such as those in research, safety, support staff, and others involved in the direct use of sharps.

Note: During inspections, OSHA will check for compliance with this provision by questioning a representative number of employees to determine if and how their input was requested.

Signs and Labels

The biohazard symbol required by the Bloodborne Pathogens Standard is fluorescent orange or orange-red, with lettering or symbols in a contrasting color.

Affix warning labels to:

- Containers of regulated biomedical waste such as liquid or semi-liquid blood and other potentially infectious materials
- Refrigerators and freezers containing materials requiring BSL-2 containment, human blood or other potentially infectious materials
- Equipment used to manipulate materials requiring BSL-2 containment, human blood, or other potentially infectious materials
- Other containers or storage areas used to collect, transport or ship this material

Affix the required labels as close as feasible to the container by string, wire, adhesive or any other method that would prevent their unintentional loss or removal.

Red bags must be used for the collection of biological waste. These bags must be marked with the universal biohazard symbol or the word “biohazard” in a contrasting color. Contaminated equipment should be labeled as to which part of the equipment is contaminated. Regulated waste that has been decontaminated does not have to be labeled.

Shipping

Shipping, transport, and receipt of biological materials can be a complex matter if dealing with infectious or potentially infectious substances. The World Health Organization offers information for shipment of biological materials at https://apps.who.int/iris/handle/10665/339825. Appendix XII lists various resources available to contact with questions about receipt and transport of regulated materials.

All biological shipments must conform to the Department of Transportation (DOT) and International Air Transport Association (IATA) requirements, as appropriate. Appendix XIII outlines such requirements for packaging and labeling of infectious materials and clinical specimen containers and can be used as guidance for preparing packages for shipment. However, any employee involved in packing, shipping, or signing manifests for these items must have DOT and IATA training as appropriate.

Cryogenics

Work with liquid nitrogen and other cryogenic liquids has potential safety hazards. If personnel are working with liquid nitrogen, which includes filling dewars or removing samples from deep freeze, wear a faceshield and cryo gloves. Do not change out liquid nitrogen tanks unless trained to do so.

Visitors and Children in Laboratories

The AbCellera Boston Policy for Visitors and Children in Laboratories can be found in the Chemical Hygiene Plan.

Personal Electronics in the Laboratories

The use of personal electronic devices such as cell phones and headphones in the AbCellera Boston laboratories is covered in Appendix XIV.

11. DECONTAMINATION

Laboratories are subject to contamination by infectious and non-infectious biological material. Frequent decontamination is necessary to provide a work area that is suitable for good microbiological practices, minimize the risk of exposure, and render contaminated material safe for handling.

There are three types of decontamination:

- Disinfection
- Sterilization
- Antisepsis

Disinfection

Disinfection is the process of using antimicrobial agents on inanimate objects to destroy a large proportion (99.999%) of non-spore forming organisms that could pose a hazard to humans or compromise an experiment. Disinfection is usually performed with a chemical agent, but heat can also be a type of disinfection treatment for liquid materials.

There are many types of chemical disinfectants used in laboratories:

- Chlorine based compounds, usually sodium hypochlorite solution (bleach)
- Alcohols, typically ethanol or isopropanol
- Glutaraldehyde solutions
- Iodophors, such as iodine
- Phenol based solutions
- Quaternary ammonium compounds

There is no universal disinfectant for all microbial agents. Some disinfectants are useful against many different types of microbes, others are used for very specific situations and agents. Various hazards exist for each type of chemical disinfectant. A risk assessment is performed for all agents in use to determine which disinfectant is effective against the agent in question, under the conditions found in the laboratory or in the given solution, at the lowest hazard to the individual using it. Appendix XV gives a broad overview of common chemical disinfectants and the types of microbe that each is effective against as well as the hazards associated with each.

Disinfectants for Work Surfaces and Reusable Items at AbCellera Boston

The following disinfectants are acceptable for work surfaces and reusable items at the prescribed concentrations:

- 10% solution of bleach (~0.5% sodium hypochlorite). The shelf life of diluted bleach is short, so bleach should be diluted fresh immediately before use, or daily at a minimum.
- 70% solution of ethyl or isopropyl alcohols. The shelf life of alcohol diluted in-house is about a month. For purchased solutions, follow the manufacturer's recommendations.

Sterilization

Sterilization refers to the destruction of all forms of life on an item or in an area. Sterilization may be accomplished using steam or gas, (e.g., steam sterilizers/autoclaves or ethylene oxide sterilizers), radiation (e.g., ^{60}Co) or a chemical (e.g., glutaraldehyde, under certain conditions). Sterilization is used to process clean, prewrapped items in which the steam or gas can penetrate to reach all areas within the packaging. Sterilization is also used for liquids, like culture media, to ensure biological experiments are accurate. The use of sterile equipment, media, and techniques prevents unwanted microorganisms from contaminating cultures.

Most equipment, media, and sometimes waste materials are sterilized in the steam autoclave. The autoclave can be used at various cycle lengths for different purposes. For example, the cycle time for dry goods sterilization will be shorter than for a liquid with a high protein load. As protein load increases, so does the cycle time for sterilization. Appendix XVI includes a guide to autoclave use and safety.

Ethylene oxide sterilizers are commonly used in the healthcare industry for implants and other medical equipment. Ethylene oxide is a toxic gas and regulated by OSHA. There are guidelines in place to use ethylene oxide sterilizers safely and to keep exposure below the OSHA Permissible Exposure Limit.

Antisepsis

Antisepsis is the application of a liquid chemical antimicrobial agent to living human or animal tissue. This chemical agent is intended to inhibit or destroy the growth of potentially infectious organisms. Handwashing with soap after exposure to a biological material is an example of antisepsis.

12. REGULATED WASTE

Sharps

Needles, scalpels, glass Pasteur pipettes, plastic serological pipettes, pipette tips, broken glassware, and any other material which would puncture biohazard bags are placed in a puncture resistant, rigid receptacle. There are two types in the laboratories: a floor model and a bench-top model. All sharps containers are red in color and labeled with the Universal Biohazard Symbol.

The Project Manager/Biosafety Officer picks up full, sealed containers from the laboratories as needed.

Red Bag Medical Waste

Dry waste that is contaminated with biohazardous material is considered red bag waste. This includes all paper, plastic, petri dish cultures, test tubes and conical tubes. No loose sharps are allowed in red bag waste and only a very limited quantity of liquid is allowed. Trace chemotherapy agent waste is allowed in red bag waste, however these boxes must be labeled for incineration only. Check with the waste hauler for specific instructions. Full, sealed disposable bench-top sharps containers may be disposed of in red bag waste. All red bag waste is placed in a cardboard Veolia receptacle with the Universal Biohazard Symbol on it. Plastic, flip top lids are required on the boxes in the BSL-2 laboratories.

The Project Manager/Biosafety Officer picks up full, sealed containers from the laboratories as needed.

Liquid Waste

The following disinfectant is approved for liquid waste decontamination at the prescribed concentrations:

- Bleach to a final concentration of 10% (~0.5% sodium hypochlorite) in liquid waste. This disinfectant is best for human source materials. If the protein load is high in the liquid waste that is being disinfected, a 20% final concentration (~1% sodium hypochlorite) is necessary. Waste containing no other hazardous chemicals may be sink disposed after a minimum contact time of 30 minutes.

Liquid waste containing no chemical components may also be autoclaved prior to sink disposal. Each cycle and its parameters must be recorded in the biological waste logbook. Quarterly challenge testing must be performed, and maintenance records kept for the autoclave. There is currently no plan to use this method of disinfection at AbCellera Boston.

All in-house methods of biotechnology-byproduct effluent treatment must be approved by the IBC. The biological waste log must be filled out for both solid and liquid waste (collected in batch), to comply with the Massachusetts Sanitary Code (105 CMR 480.000).

Glass

Place non-hazardous, non-contaminated intact and broken glass in the blue and white cardboard containers labeled as “CLEAN, BROKEN GLASS DISPOSAL”. Do not pick up broken glassware directly with the hands – use long forceps or dustpan/scrapers and decontaminate these items must after use. **NO BIOHAZARDOUS AGENTS** are allowed in the blue and white glass bins.

Regular Trash

No biohazards, chemicals, broken glass, sharps, or gloves are allowed in regular trash receptacles.

13.

TRAINING

General Biosafety

Supervisors must ensure that employees with occupational exposure to biological materials participate in a training program that is provided at no cost to the employee. Employees will complete the training at the time of initial assignment to tasks where occupational exposure may take place, or when there is a change in an employee's responsibilities, procedures, or work situations which places them at risk of such exposure, and at least annually thereafter.

Annual training will be provided by the Biosafety Officer or designee**.**

Training aids may consist of PowerPoint slides, copies of in-house policies, and other written materials to supplement the training.

Biosafety training covers:

- An overview of biosafety, including biohazards, risk groups and biosafety levels
- Available biosafety resources
- Risk assessment
- Standard practices for working in BSL-1 and BSL-2 laboratories
- NIH Guidelines around the use of recombinant DNA
- Aerosol control, aspiration filters, and use of the biosafety cabinet
- Using sharps safely
- Spill response
- Exposure response
- Biowaste management

Training materials are located in the central safety files.

Copies of all policies and procedures as outlined in this manual are available electronically in the B-drive in the Boston All Safety Folder.

Bloodborne Pathogens

All employees working with human source materials or OPIM must receive training on Bloodborne Pathogens upon employment or assignment to tasks involving the potential for occupational exposure. The training should include an opportunity for interactive questions and answers with the person conducting the training session. OSHA requires annual retraining within one year of the previous training.

The specifics of Bloodborne Pathogens Training are given in Appendix XVII.

14. RECORDKEEPING

Training Records

All training sessions are documented in writing with training records kept in the main safety files for at least 3 years from the date of the training. The training record includes dates of training sessions, content of training sessions, names of persons conducting training sessions, and the name, signatures and job titles of all persons attending training sessions. Training records are maintained by the Project Manager/Biosafety Officer or designee.

Medical Records

Mount Auburn Occupational Health Services keeps confidential medical records for employees with occupational exposure for the duration of their employment plus 30 years. Medical records include:

- Employee's name and social security number
- Employee's hepatitis B vaccination status, including vaccination dates and any medical records related to the employee's ability to receive vaccination
- Results of examinations, medical testing, post-exposure evaluation and follow-up procedures
- Written opinions of healthcare professionals
- Copies of information provided to healthcare professionals

OSHA Recordkeeping

An exposure incident is evaluated to determine if the case meets OSHA's Recordkeeping Requirements (29 CFR 1904). This determination and the recording activities are done by a Human Resources representative or designee.

Sharps Injury Log

The sharps injury log must be maintained in a manner that protects the privacy of employees. At a minimum, the log contains the date and time of the incident, the type and brand of device involved in the incident, location of the incident, and description of the incident. Appendix XVIII contains the AbCellera Boston Sharps Injury Log.

Safer Sharps Program

The Needlestick Prevention Act and Bloodborne Pathogens Standard require employers to evaluate safer sharps when used with human source materials (see section 10, Work Practices, for details of the program). The Safer Sharps Program documents employee questionnaires and physically evaluates newly engineered products on the market. The employer provides the employee with the safest sharp appropriate for the job function at no cost to them.

15. MEDICAL SURVEILLANCE AND VACCINATIONS

Occupational Health Center

Mt. Auburn Occupational Health Services is the occupational health provider for AbCellera Boston.

- Phone number: (617) 354-0546
- Address: 725 Concord Avenue, Suite 5100, Cambridge, MA 02138
- Hours: Monday through Friday, 8:00am to 12:00pm, 1:00pm to 4:00pm

All medical evaluations and procedures, including the Hepatitis B vaccine and vaccination series, post-exposure evaluation and follow-up, and prophylaxis, are made available at no cost to the employee.

Hepatitis B Vaccination

AbCellera Boston makes the Hepatitis B vaccination series available to all employees who may potentially have occupational exposure and extends post-exposure evaluation and follow-up to all employees who have had an exposure incident.

Appendix XIX contains the AbCellera Boston Hepatitis B vaccination form. All employees with anticipated exposure to blood, tissue or OPIM must accept or decline the vaccine and sign the form.

Employees receiving the Hepatitis B vaccine will follow procedures as outlined and required by the occupational health provider.

The vaccination series is administered by a nurse or practitioner at the occupational health provider. The vaccination is safe and effective and given as a 3 shot series with titer at no cost to the employee.

The Project Manager/Biosafety Officer has the responsibility to ensure that the vaccination is offered within 10 days of the employee falling under the Bloodborne Pathogens Standard, and declinations are documented appropriately.

Post-Exposure Evaluation and Follow-Up

The occupational health provider will provide post-exposure evaluation, treatment, and follow-up, after the report of an exposure incident.

Report all exposures immediately to your supervisor and the Biological Safety Officer. In addition, you must complete an incident report within 24 hours. The AbCellera Boston incident

report can be found in an appendix of the Emergency Action Plan and in the Red Emergency Binders.

After decontamination, travel by car or ambulance to occupational health or the emergency room for evaluation and treatment of the exposure.

A healthcare professional's written opinion may be obtained when an employee is sent to obtain the Hepatitis B vaccine and whenever an employee is sent to a healthcare professional following an exposure incident. Written opinions will follow the health provider's policy.

All medical records relating to post-exposure evaluation and follow-up are confidential.

The occupational health provider will monitor post-exposure policy effectiveness and maintain records related to this policy.

Serum Storage Medical Surveillance

The occupational health provider will provide serum storage for those employees designated for medical surveillance. Contact the occupational health provider to evaluate situations that may warrant serum storage. Due to logistical issues with serum storage, most occupational health centers rely on baseline testing at the time of exposure.

16.

EMERGENCY RESPONSE

It is important to summon help immediately in the event of a medical emergency or life-threatening exposure incident. For any emergency that is life threatening:

1. Yell “help” to get another person to aid in the situation
2. Dial 911 to get immediate help from emergency responders

Report all emergencies immediately to the employee’s supervisor. Report biological exposure emergencies to the Biological Safety Officer as well.

Resource Information

Red Emergency Binders include information on emergency response, evacuation response and biological spill response, among other things. Use the Red Emergency Binder if there is an emergency and immediate action must be taken.

An emergency phone list is posted by all laboratory phones. The list includes the contact information for various emergency services, including:

- Hospital emergency room information
- Occupational Health contact and fax numbers
- Emergency Coordinator contact information
- Safety Officer contact information
- Safety Consultant contact information, if applicable
- Spill contractor information

Exposure Response

Immediate response to a biological exposure is necessary to prevent possible infection.

If an exposure to a biological material occurs, it is important to identify the material immediately and obtain a sample for evaluation if it has not been previously tested. If testing data is available in the safety records or from the supplier, obtain the results immediately.

In general, follow the guidelines below for immediate response to biological exposure:

Eye Splash	Hold eye open at eyewash station. Flush eye for 15 minutes
Needlestick	Use soap and wash exposed area for 15 minutes in a laboratory sink. Report immediately and call/go to Occupational Health or the ER for consultation.
Skin Exposure	Use soap and wash exposed area for 15 minutes in a laboratory sink or safety shower

Open Wound Exposure	Rinse well with clean water
Mucous Membrane Exposure	Rinse area to the best of your ability with clean water
Exposure to Clothing:	Remove contaminated clothing, cutting it off to prevent spread of contamination if necessary. If material has soaked through to the skin, wash affected skin as explained above.

Report all overt exposures from parenteral inoculation and/or exposure to mucous membranes immediately to your supervisor and the Biological Safety Officer. Promptly seek medical attention for any exposures of this type, but especially for exposures to human source materials. Counseling regarding the risk of infection should be given by a medical professional, either at the emergency room, or Occupational Health Center.

Report all exposures on an incident report form within 24 hours of the incident. Incident report forms can be found in an appendix of the Emergency Action Plan and in the Red Emergency Binders.

Consult a medical professional as soon as possible after exposure for counseling. The medical professional may suggest Hepatitis B vaccination or prophylaxis following exposure to human source materials or may suggest beginning a drug regimen to minimize the chance of HIV seroconversion, which must be given within a short time after exposure to known HIV positive material.

17. SPILLS

Spill supplies for biological spill cleanup can be found in the Main Laboratory and in the Tissue Culture Room. Supplies for biological spills include:

- At least 1 gallon of bleach
    - Periodically check the date on all bleach bottles to be used for spill cleanup to ensure that they are not expired
- Other appropriate disinfectant if bleach is not a proper disinfectant for the material you are using. Bleach is not effective for every type of biological hazard but is useful for most.
- Paper towels or other absorbents
- Biohazard bags must be available to contain spill materials
- Forceps or a dustpan and broom must be available to pick up contaminated sharps items, such as needles, broken glass or broken, rigid plastic items

PPE such as a lab coat, gloves, and face shield or goggles should be available in the laboratory.

Containing biological spills, and especially aerosols produced by a spill, is extremely important to the safety of individuals cleaning a spill. Precautions must be taken to avoid spreading contamination while performing biological spill cleanup. Dispose of all waste produced from the cleanup as biological hazardous waste.

Spills at BSL-1

1. Remove contaminated Personal Protective Equipment (PPE)
2. Wash hands and exposed skin immediately if you have been exposed to the spill
3. Personal Protective Equipment (PPE) must be worn during spill cleanup. A lab coat, safety glasses, and gloves are required. Booties, goggles and face shields should be used as necessary, depending on the volume of the spill and the possibility for splash, splatter or aerosols.
4. Assemble the spill kit materials before attempting spill cleanup
5. Surround the spill with regular strength bleach (~5% sodium hypochlorite) so that the disinfectant can be mixed into the spill using paper towels. A ring of bleach around the spill will keep the spill from spreading.
6. Place absorbent materials like paper towels over the spill. The paper towels will reduce any splash or splatter that may occur if you added the disinfectant directly into the spill.

7. Add bleach over the paper towels to produce an estimated volume to volume concentration of 1:10, bleach to spill ratio
8. Allow contact time of 30 minutes for disinfection of the spill
9. Wipe up the spill and dispose of used cleanup materials in the biohazard waste containers
10. Dispose of any sharps into puncture resistance sharps containers. Remove any sharps or broken glass by an indirect method, such as tongs, a dustpan and broom or a scoop. Never pick up sharps with your hands.
11. Clean the spill area with a soapy solution after all materials have been picked up and placed in the appropriate waste containers. This step is necessary to remove any protein substances left on surfaces from the spill.
12. Clean the area one more time with a freshly prepared 10% bleach solution (~0.5% sodium hypochlorite). A 10% bleach solution can be prepared by adding 100 ml of regular strength household bleach to 900 ml of water. If using industrial strength bleach, read the label and dilute accordingly to a final concentration of 5,000 ppm chlorine. (Most household bleach is 52,500 ppm chlorine).
13. Follow with a final rinse of water or 70% ethyl or isopropyl alcohol to remove bleach residue
14. Disinfect or autoclave reusable items used in spill cleanup prior to returning them to the biological spill kit location

Spills at BSL-2

For spills of materials requiring BSL-2 containment, or any BSL-1 spill that may produce aerosols, use the above listed BSL-1 spill procedures plus:

1. Leave the laboratory quickly and evacuate all personnel from the laboratory. Close the door and post a "no entry" sign.
2. Put any contaminated lab coats and clothing in a red biohazard bag before leaving the laboratory if it is safe to do so. Seal the biohazard bag and label it with your name, date, and identity of the contents. Contact the Biosafety Officer about the spill and potential contamination. Contaminated clothing will need to be autoclaved before being sent to the launderer.
3. Allow 30 minutes for aerosols to settle before reentering the laboratory and proceeding with cleanup
4. Contact your Supervisor, Biosafety Officer, and a Safety Team Member to discuss the logistics of cleanup
5. Always wear personal protective equipment, including a lab coat, gloves and safety glasses. Booties, a face shield or goggles may be appropriate depending on the volume of the spill.

6. While cleaning the spill, avoid splashing or splattering the materials, which can produce aerosols

Spills in a Biosafety Cabinet (BSC)

The main protection from biological spills in a BSC is the HEPA filter. If there is a spill in the BSC, check the operation of the HEPA filter by looking at the gauge before attempting any spill cleanup. Make sure the gauge indicates that the filter is operating appropriately (see section 9, “Engineering Controls”, for an explanation of how to check the operation of the BSC).

1. Put on clean gloves, a lab coat and safety glasses. Proceed with decontamination while the cabinet continues to run.
2. Spray down cabinet surfaces and equipment with the preferred disinfectant and wipe all surfaces. If using bleach, follow these procedures with a water or 70% ethyl or isopropyl alcohol rinse to reduce corrosion of the metal surfaces.
3. If possible, lift the front exhaust grille and tray, spray with disinfectant and wipe. If you cannot lift the front grill, flood the drain pan beneath the work surface with disinfectant and allow 30 minutes contact time before draining.
4. Call the Project Manager/Biosafety Officer if the spill is inaccessible or contaminates a filter.

Large Scale Spills (BSL-1 >10 L)

1. Wash hands and exposed skin immediately if you have been exposed to the spill.
2. Leave the laboratory and evacuate all personnel from the laboratory. Close the door and post a "no entry" sign.
3. Contact the Biosafety Officer and Emergency Coordinator to plan the cleanup, including notification to Veolia.
4. The Biosafety Officer or designee will determine if there is a need to call the Arlington Board of Health.

Biological Mixed Spills

In general, treat biological mixed spills as follows:

- Biological and chemical spills: Use a disinfectant that is compatible with the spilled chemical to kill the biological material and then treat as a chemical spill

Consult the Biosafety Officer and Chemical Hygiene Officer for all mixed spills.

Spill Reporting

Report all spills on an incident report form within 24 hours of the incident. Refer to the "Accident/Incident Report" paragraph in Section 6 "Recombinant and Synthetic Nucleic Acid Molecules" for additional Arlington reporting requirements.

APPENDIX I: DEFINITIONS

Amphotropic	A pathogen that does not produce disease in its natural host, but does replicate in tissue culture cells of the host species and in cells from other species
ANSI	American National Standards Institute, a private non-profit organization that oversees the development of voluntary consensus standards for products, services, processes, systems, and personnel in the United States and coordinates U.S. standards with international standards so that American products can be used worldwide
Biosafety Officer	Also known as Biological Safety Officer or BSO, oversees and gives safety input for all biological work done in the facility. See section 2 for site specific details.
BSL	Biosafety Level, a designation outlining work practices used to avoid employee exposures and contamination of the environment with biohazards
Blood	Human blood, blood components, and products derived from blood
Bloodborne Pathogens (BBP)	Pathogenic microorganisms that are present in human blood and can cause disease in humans. These pathogens include, but are not limited to: • Hepatitis B virus (HBV) • Hepatitis C virus (HCV) • Human immunodeficiency virus (HIV).
BMBL	Biosafety in Microbiological and Biomedical Laboratories, a publication by the U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, and National Institutes of Health outlining standard practices for the use of biologicals in laboratories
BSC	Biosafety cabinet, an engineering control used to establish a sterile environment for working with biological specimens which also protects workers from exposure
CDC	Centers for Disease Control and Prevention, the United States' health protection agency which protects people from health, safety, and security threats.
EBV	Epstein-Barr Virus, a member of the herpesvirus family that can infect humans
Ecotropic	A pathogen that can replicate or reproduce in cells of both the host species and a narrow range of other species
Etiologic	Cause or origin of disease
Exposure Incident	A specific eye, mouth, other mucous membrane, non-intact skin, or parenteral contact with blood or other potentially infectious or biohazardous material that results from the performance of an employee's duties

Human Cell Line	An in vitro or animal-passaged culture or human cells that fulfill traditional requirements of a cell line designation. That is, the cells are immortalized cells, transformed by spontaneous mutation or natural or laboratory infection with an immortalizing agent such as Epstein-Barr virus (EBV). Note: EBV is a bloodborne pathogen.
Human Cell Strain	Cells propagated in vitro from primary explants of human tissue or body fluids which have finite lifetime (non-transformed) in tissue culture for 20-70 passages. Human cell "strains" must be handled as potential biohazards unless characterized by testing to be free of bloodborne pathogens.
Hybridoma Cell Line	Immortalized cell lines created by fusion of primary cells with a continuous cell line
Luer Lock	An engineering control used to make leak-free connections; often used with needles and syringes preventing separation of the two parts and potential needlesticks
Murine	Relating to, affecting, resembling, or derived from a rat or mouse
Needleless Systems	Devices, for various procedures, that provide an alternative to needles and reduce the risk of injury involving contaminated sharps. Examples include: • IV medication systems which administer medication or fluids through a catheter port using non-needle connections • Jet injection systems which deliver liquid medication beneath the skin or through a muscle
NIH	The National Institutes of Health (NIH), a part of the U.S. Department of Health and Human Services, is the nation's medical research agency
NSF	NSF International, formerly the National Sanitation Foundation. NSF certifies the design, construction and performance of biosafety cabinets to NSF/ANSI 49 and provides biosafety cabinet field certifier accreditation
Occupational Exposure	Reasonably anticipated skin, eye, mucous membrane, non-intact skin, or parenteral contact with blood or other potentially infectious or biohazardous material that may result from the performance of an employee's duties
Oncogenic	Causing or tending to cause the formation and development of tumors
Oncovirus	An RNA tumor virus
Organoids	Cell-derived in vitro 3D organ models that allow the study of biological processes
Other Potentially Infectious Materials (OPIM)	• Body fluids and secretions including semen, vaginal, cerebrospinal, synovial, pleural, pericardial, peritoneal, and amniotic; saliva in dental procedures, and any body fluid that is visibly contaminated with blood, and all body fluids in situations where it is difficult or impossible to differentiate between body fluids • Any unfixed tissue or organ other than intact skin from a human, living or dead • HIV-containing cell or tissue cultures, organ cultures, and HIV or HBV containing culture medium or other solutions; and blood, organs or other tissues from experimental animals infected with HIV or HBV

Parenteral	Administered by some means other than oral or rectal intake, particularly intravenously or by injection
PI	Principal Investigator, the lead researcher for project such as a laboratory study or a clinical trial
Polytropic	A pathogen that can replicate or reproduce in cells of both the host species and other species
Recombinant or Synthetic Nucleic Acid Molecules	(i) molecules that a) are constructed by joining nucleic acid molecules and b) that can replicate in a living cell, i.e., recombinant nucleic acids (ii) nucleic acid molecules that are chemically or by other means synthesized or amplified, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids (iii) molecules that result from the replication of those described in (i) or (ii) above
Replication Competent	Able to replicate or reproduce
Safety Committee	An organizational structure where members represent all affected groups within the company to ensure that safety issues are addressed. This gives everyone a voice and should include an effective number of participants to address and enforce all issues.
Safer Sharps	Also called Sharps with Engineered Sharps Injury Protections. Non-needle sharps or needle/scalpel/knife devices which contain built-in safety features that are used for collecting fluids, administering medications or other fluids, or for other procedures that involve the risk of sharps injury. This description covers a broad array of devices, including: • Syringes with a sliding sheath that shields the attached needle after use • Needles that retract into a syringe after use • Shielded or retracting catheters • Intravenous medication (IV) delivery systems that use a catheter port with a needle housed in a protective covering • Retractable blade scalpel or Exacto knife
Universal Precautions	An approach to infection control whereby all human blood and certain human body fluids are treated as if known to be infectious for HIV, HBV, HCV, and other bloodborne pathogens
Xenotropic	A pathogen that can replicate or reproduce only in cells other than those of the host species

APPENDIX II: SUMMARY OF RECOMMENDED BIOSAFETY LEVELS FOR INFECTIOUS AGENTS

BSL	Agents	Practices	Primary Barriers and Safety Equipment	Facilities (Secondary Barriers)
1	Not known to consistently cause diseases in healthy adults	Standard microbiological practices	• No primary barriers required • PPE: laboratory coats and gloves; eye, face protection, as needed	Laboratory bench and sink required
2	Agents associated with human disease Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure	BSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual defining any needed waste decontamination or medical surveillance policies	• BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials • PPE: Laboratory coats, gloves, face and eye protection, as needed	BSL-1 plus: • Autoclave available
3	Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure	BSL-2 practice plus: • Controlled access • Decontamination of all waste • Decontamination of laboratory clothing before laundering	• BSCs or other physical containment devices used for all open manipulations of agents • PPE: Protective laboratory clothing, gloves, face, eye and respiratory protection, as needed	BSL-2 plus: • Physical separation from access corridors • Self-closing, double-door access • Exhausted air not recirculated • Negative airflow into laboratory • Entry through airlock or

				anteroom • Hand washing sink near laboratory exit
4	Dangerous/exotic agents which post high individual risk of aerosol-transmitted laboratory infections that are frequently fatal, for which there are no vaccines or treatments Agents with a close or identical antigenic relationship to an agent requiring BSL-4 until data are available to redesignate the level Related agents with unknown risk of transmission	BSL-3 practices plus: • Clothing change before entering • Shower on exit • All material decontaminated on exit from facility	• All procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure suit	BSL-3 plus: • Separate building or isolated zone • Dedicated supply and exhaust, vacuum, and decontamination systems Other requirements outlined in the text

Reference: Biosafety in Microbiological and Biomedical Laboratories, CDC/NIH

APPENDIX III: PROCEDURES FOR BSL-2 ENHANCED (BSL-2+)

There is currently no BSL-2+ work conducted at AbCellera Boston. If there is a need in the future, procedures will be developed after conducting a risk assessment.

APPENDIX IV: ARLINGTON BIOSAFETY AND RECOMBINANT DNA REGULATIONS

SECTION 1: AUTHORITY

On April 11, 2012 the Arlington Board of Health, pursuant to the authority granted under Massachusetts General Laws (M.G.L.), Chapter 111, Section 31, voted to adopt the "**Biosafety and Recombinant DNA Regulations**" to protect the public health of the community.

SECTION 2: APPLICABILITY/ PURPOSE

These regulations shall apply to all research, production, and other associated activities involving rDNA materials or Biological Agents undertaken within the Town of Arlington, Massachusetts. All such activities shall be undertaken only in strict conformity with these regulations and with current National Institutes of Health (NIH) Guidelines (hereinafter referred to as the "Guidelines") as defined below herein § 3. Any institution engaged in research or production involving rDNA materials or Biological Agents shall also comply at all times with any other applicable federal and state regulations covering such work, including regulations promulgated by the Centers for Disease Control (CDC), Occupational Safety Health Administration (OSHA), Environmental Protection Agency (EPA) Massachusetts Department of Environmental Protection (MADEP) and Massachusetts Department of Public Health (MADPH).

These regulations are promulgated to ensure proper safe guards are in place for work with Biological Agents and recombinant DNA (rDNA) within the Town of Arlington. These regulations promote the safe and responsible conduct of science by institutions utilizing Biological Agents and rDNA materials, and promote competency and adequate training of laboratory staff in laboratory safety.

SECTION 3: DEFINITIONS

Biological agent: any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, or anything capable of causing death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment. [from the CDC Select Agents and Toxins Final Rule. 42 CFR § 73.1 Definitions]

BMBL: Biosafety in Microbiological and Biomedical Laboratories. The key recommendations for working with biological materials in the United States (US) published jointly by the CDC and the NIH.

BSL: Biological safety level. There are four biosafety levels which consist of combinations of laboratory practices and techniques, safety equipment, and laboratory facility containment. Each combination is specifically appropriate for the operations performed the

documented or suspected routes of transmission of the infectious agents, and the laboratory function or activity.

Biosafety Level One Laboratory (BSL-1): All facilities that meet or exceed the criteria for Biosafety Level 1 containment, according to descriptions in the BMBL; appropriate for agents that are not known to cause disease in normal, healthy humans.

Biosafety Level Two Laboratory (BSL-2): All facilities that meet or exceed the criteria for Biosafety Level 2 containment, according to descriptions in the BMBL; appropriate for handling moderate-risk agents that cause human disease of varying severity by ingestion or through percutaneous or mucous membrane exposure.

Biosafety Level Three Laboratory (BSL-3): All facilities that meet or exceed the criteria for Biosafety Level 3 containment, according to descriptions in the BMBL; appropriate for agents with a known potential for aerosol transmission, for agents that may cause serious and potentially lethal infections and that are indigenous or exotic in origin

Biosafety Level Four Laboratory (BSL-4): All facilities that meet or exceed the criteria for Biosafety Level 4 containment, according to descriptions in the BMBL; appropriate for exotic agents that pose a high individual risk of life-threatening disease by infectious aerosols and for which no treatment is available

CDC: Centers for Disease Control and Prevention

EPA: Environmental Protection Agency

Guidelines: The most recent version of the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules published in the Federal Register, and any further amendments, wherever published, which are adopted by NIH, or any successor agency thereto.

In the event that the NIH shall abolish or discontinue its Guidelines, those Guidelines in effect at the time of such discontinuance shall remain in effect within the Town of Arlington until further written notice from the Board of Health.

Institution: Any single individual, group of individuals, or organization, whether public or private.

Institutional Biosafety Committee: (IBC) a committee established by an institution in accordance with the Guidelines and the terms set forth in these regulations

Large-scale: The use of more than ten liters of rDNA and/or Biological Agent culture. This threshold shall be based on the cumulative volume of culture in all vessels throughout the institution's facility, not just a single vessel or experiment.

MADEP: Massachusetts Department of Environmental Protection

MADPH: Massachusetts Department of Public Health

OSHA: Occupational Safety and Health Administration

Recombinant DNA molecules (rDNA): in the context of the Guidelines, rDNA molecules are defined as either: (i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i) above.

Select Agent: Biological materials that have been restricted by the Department of Health and Human Services (DHHS) and the Animal and Plant Health Inspectional Services (APHIS) because of a perceived risk of bioterrorism through improper possession or use. Laboratories that wish to conduct research on these materials must follow strict guidelines that include registration of the entity, laboratory, and personnel with DHHS/APHIS prior to obtaining agents and starting research.

Risk Group: NIH classification of microbiological agents based on association with and resulting severity of disease

Risk Group 1: Agents that are not associated with disease in healthy adult humans

Risk Group 2: Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available

Risk Group 3: Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available

Rick Group 4; Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available

Any other terms, not specifically defined herein, shall have the meaning as defined in the Guidelines. If the Guidelines do not define the term, it shall have the meaning as is commonly used.

SECTION 4: PERMIT REQUIREMENT

Any institution proposing to process or use Biological Agents or rDNA must obtain a permit from the Arlington Board of Health before engaging in any activity, including construction or renovation of facilities.

SECTION 5: TERMS AND CONDITIONS

1) All rDNA materials and Biological Agents classified as Risk Group 4 agents by the Guidelines, or any work with rDNA materials or a Biological Agent that requires BSL-4 containment based on a biological risk assessment shall be prohibited in the Town of Arlington.
2) Institutions applying for a permit must complete and submit the Plan Review Packet for the use of Biological Agents and/or rDNA within the Town of Arlington. The Director of Health and Human Services or his or her designee will review said application and make its recommendation to the Board of Health. A hearing with the Board of Health will be scheduled within sixty (60) days after the application is filed to take action on the application. The period within which final action shall be taken may be extended for a definite period by mutual consent of the Board of Health and applicant.
3) Each institution must designate an individual as the point of contact for the permit process. This person may be the biosafety officer or responsible official or may serve the institution in another capacity.
4) Institutions must comply with this regulation and the Guidelines at all times.
5) Institutions must allow inspections of both facilities and records, as related to these regulations, in response to emergencies and at other times deemed necessary by the Board of Health.

6) All areas in which rDNA or Biological Agents are utilized shall be free of rodent and insect infestation.
7) Institutions must adhere to a Health and Safety Manual, prepared by the institution, which contains all procedures relevant to the use of Biological Agents and rDNA at all levels of containment at use at the institution. The manual shall also contain a plan for waste disposal in compliance with all applicable federal, state, and local laws or regulations.
8) Institutions must establish and implement a training program of safeguards and procedures for both laboratory personnel using Biological Agents and/or rDNA and non-laboratory personnel who may come into contact with these materials.
9) Each institution shall establish an Institutional Biosafety Committee (IBC) which shall meet at least annually. The IBC shall be established in accordance with the Guidelines defined above, except that the required composition of each IBC shall include at least one representative from the Town of Arlington, approved by the Board of Health. The community member of the IBC shall have no financial interest in the institution or any other institution in competition therewith, and such representative shall be bound to the same provisions as to nondisclosure and nonuse of proprietary information as all other members of the IBC, except to the extent necessary to alleviate any public health hazard.
10) In accordance with the Guidelines, the IBC, acting on behalf of an institution, shall review all rDNA and Biological Agent use for compliance with the Guidelines and approve those projects that conform to the Guidelines. A description of each protocol approved by the IBC, including all organisms and the containment to be used, and a statement certifying that the experiment conforms with the Guidelines shall be filed with the Board of Health.
11) All institutions shall provide an appropriate medical surveillance program as determined by their IBC and consistent with the Guidelines. Each institution shall submit a description of its medical surveillance program and documentation regarding its implementation as part of its annual report.
12) Each institution shall complete an annual report by April 30 of each year. Said reports must include a summary of the work performed over the past year and addressing any ongoing work and in addition the following:
    a. Current list of IBC members
    b. Copies of the previous year's IBC meeting minutes
    c. Summary of research and any changes in the past year
13) All information sent to the Board of Health shall have all proprietary information and trade secrets removed therefrom. The full text shall remain on file in the records of the institution for inspection at all reasonable times by any member of the IBC or The Board of Health or its designee(s). The Board of Health and its designee(s) shall maintain the confidentiality of all proprietary information and trade secrets released to them by reason of these regulations to the extent permitted by law. As used in these regulations, proprietary information and trade secrets shall be defined as set forth in under the laws of the commonwealth of Massachusetts.
14) Every applicant shall submit evidence of, and maintain at all times while conducting activities regulated hereunder, a policy or policies of insurance against liability arising out of activities regulated hereunder, for general liability insurance, and contractual liability insurance covering any indemnification required hereunder or by separate agreement, each in an amount of at least $1,000,000 for personal injury or death to any one person, and at least $5,000,000 for personal injury or death from any one incident, and at least $1,000,000 for property damage, and in addition, the institution shall have in full force

and effect any other particular or special policy of insurance required by law and the Town of Arlington shall be named as an additional insured in all such policies.

15) Each institution engaging in, or intending to engage in, any activities regulated hereunder agrees to indemnify, defend, protect, and hold harmless the Town of Arlington, its selectmen, officers, agents and employees from and against any and all claims, demands, losses, damages, liabilities, fines, charges, penalties, administrative and judicial proceedings and orders, judgments, remedial actions of any kind, all costs and cleanup actions of any kind, and all costs and expenses incurred in connection therewith, including reasonable attorney's fees and costs of defense (collectively, the "losses"), directly or proximately resulting from the institution's negligence with regard to any acts, omissions or conduct in any way related to any activity regulated hereunder, pursuant to its permit, its application therefore, or resulting from the institution's failure to comply with the terms of the permit, the Regulation of the Guidelines.
16) Permits shall be issued and renewed on an annual basis. The fee for issuance and renewal of permits will be set by the Town Manager.

SECTION 6: LARGE SCALE USE

1) Any institution intending to use Biological Agents or rDNA on a large scale requires the expressed written approval of the Arlington Board of Health prior to conducting any such activity.
2) Any currently permitted institution shall request approval to conduct large scale activity from the Board of Health at least thirty (30) days prior to the initiation of any large scale-related activity, which may include, but not be limited to, construction or renovation of facilities. The Board of Health shall act and make a decision on the request within a thirty (30) day period from receipt of the request. Approval request should come in the form of proposed floor plan of the large scale room and IBC application documenting the proposed research and risk assessment by the Biosafety officer/IBC committee. A formal presentation to the Board of Health may be required to review the materials submitted prior to the Board of Health making a final decision to approve the project(s).
3) Institutions which are not currently permitted shall request approval to conduct large scale activity as part of their application for a Biological Agent or rDNA use permit.
4) During the review of the institution's request, the Board of Health may request additional information from the institution pertaining to the proposed large scale activity.

SECTION 7: EMERGENCY RESPONSE

1) The institution shall report immediately, and in no case more than twenty-four (24) hours, to the Board of Health and any other appropriate authorities any significant problems with or violations of the Guidelines or these regulations, any significant Biological Agent or rDNA- related accidents or illnesses, and any accidental release representing a significant hazard to employees or the public. The initial report shall be provided verbally to the Board of Health, with a written report documenting the initial report to follow within 24 hours. The institution shall provide a final written report to the Board of Health within 30 days of the initial report. The final written report shall include, but not be limited to, information detailing causes, outcomes, response measures, corrective actions and subsequent preventive measures related to the incident.
2) The institution shall provide a plot plan showing the location of all facilities, and a floor plan showing the internal layout of all facilities.

3) The institution shall submit a plan for orienting representatives of the Health, Police and Fire Departments to the facilities and the procedures to be utilized in the event of an emergency.

SECTION 8: ENFORCEMENT

Enforcement of this Regulation shall be the duty and responsibility of the Arlington Board of Health or its designee(s).

SECTION 9: PENALTIES

1) A violation of any condition or restriction of a permit or provision of these regulations shall subject the violator to a fine of three hundred ($300) dollars, or by a criminal complaint in a court of competent jurisdiction. Each day on which any violation exists shall be deemed to be a separate and distinct offense.

2) Once a permit has been issued it may be revoked, suspended, or modified, by the Board of Health, or not renewed upon a determination, after due notice and hearing, that the institution involved has materially failed to comply with these regulations or the permit requirements, and terms and conditions, including adherence to the Guidelines.

3) Notwithstanding the above, the Board of Health, upon determination that any violation constitutes an immediate or severe threat to the public health and safety, may order the necessary remedial actions up to and including the immediate closure of any premises or laboratory engaging in or contributing to such threat, without prior notice and hearing but with subsequent notice and hearing within reasonable time.

SECTION 10: EXCLUSIONS

The provisions of this Regulation are not intended to apply to clinical, non-research operations of doctors, dentists and veterinarians within the Town of Arlington when governed by other local, state and federal agencies and regulations.

SECTION 11: SEVERABILITY

The provisions of this section are severable; and if any of the provisions of these regulations shall be held unconstitutional or otherwise invalid by any court of competent jurisdiction, the decision of such court shall not affect or impair any of the remaining provisions.

APPENDIX V: RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES PROJECT REGISTRATION FORM

Institutional Biosafety Committee

91 Mystic Street, Arlington, MA

Project Number:	
Project Title:	
Initiation Date:	
Last Update:	
Principal Investigator:	
Address:	
Phone:	
Email:	

The signatures below represent the acceptance of responsibility for completeness of this project registration form, and compliance with all local, state, and federal regulations and laws pertaining to the use of recombinant or synthetic nucleic acid molecules covered under this protocol. Copies of this protocol must be provided to the individuals working under it and to other AbCellera Boston staff as requested or required.

Principal Investigator's Signature: _____ Date: _____

Program Director's Signature: _____ Date: _____

This protocol has been reviewed and accepted by the AbCellera Boston Institutional Biosafety Committee (IBC). Please note that approval is not final until the principal investigator receives written confirmation of the approval.

IBC Chairperson's Signature: _____ Date: _____

A. Project Classification

Please review the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules and then check the appropriate level for this project registration in the chart below. Consult with BSO/Safety to confirm projects under III-E or III-F.

Check	Level	Approval/ Review	Examples
	III-A	NIH Director, IBC	The deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally, if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture.
	III-B	NIH/OSP, IBC	Experiments involving the cloning of toxin molecules with LD_{50} of less than 10 nanograms per kilogram body weight. Experiments that have been approved (under Section III-A-1-a) as major actions under the NIH Guidelines.
	III-C	IRB, IBC	Experiments involving the deliberate transfer of recombinant or synthetic nucleic acid molecules, or DNA or RNA derived from recombinant or synthetic nucleic acid molecules, into one or more human research participants.
	III-D	IBC†	Experiments using Risk Groups 2, 3, 4 agent, or restricted agents as host-vector systems. Experiments in which DNA from Risk Groups 2, 3, 4 agents, or restricted agents is cloned into nonpathogenic prokaryotic or lower eukaryotic host-vector systems. Experiments involving the use of infectious DNA or RNA viruses or defective DNA or RNA viruses in the presence of helper virus in tissue culture systems. Experiments involving whole animals. Experiments involving more than 10 liters of culture. Experiments involving influenza viruses.
	III-E	IBC§	Experiments involving the formation of recombinant or synthetic nucleic acid molecules containing no more than two-thirds of the genome of any eukaryotic virus. Experiments involving transgenic rodents.
	III-F	Exempt	Synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell and (2) are not designed to integrate into DNA, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight. Experiments that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature. Experiments that consist entirely of nucleic acids from a prokaryotic host, including its indigenous plasmids or viruses when propagated only in that host (or a closely related strain of the same species), or when transferred to another host by well-established physiological means. Experiments that consist entirely of nucleic acids from a eukaryotic host including its chloroplasts, mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species). Genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA.

† Approval required before initiation.

§ Notify IBC when project is initiated. IBC approval required.

The full description for each level can be found in the NIH Guidelines: **https://osp.od.nih.gov/wp-**

content/uploads/NIH_Guidelines.pdf

B. Project Goals

Please give a brief summary of project goals stated in non-technical terminology.

Insert text here

C. Technical Description of Experiments

Provide a technical description of experiments. Include enough detail that referencing other documents or scientific papers is not necessary.

Insert text here

C.1. What is the source of the nucleic acids?

Include gene names and organism of origin.

Insert text here

C.2. What is the nature of the nucleic acid segment to be inserted?

Does the insert code for a toxin, what percentage of viral genome is eukaryotic, etc.?

Insert text here

C.3. What hosts and/or vectors will be used?

List all prokaryotic and eukaryotic hosts.

Host/Vector	Source of Material (Vendor/Institution)	Description

C.4. Will non-recombinant microorganisms be used?

Describe other potential sources of microorganisms, such as etiologic agents, blood, tissues, etc.

Insert text here

C.5. What is the scale of work?

Bench scale <9.9 liters, or production scale >9.9 liters

Insert text here

C.6. Will animals be used under this project registration?

Outline procedures for which animal use is required. IACUC review will be necessary for any experiments involving animals.

If yes, specify:

Host
Vectors
Inserted DNA
What fraction of eukaryotic viral genome is contained in the recombinant molecule?

C.7. Will plants be used under this project registration?

If yes, specify:

Host
Vectors
Inserted DNA
What fraction of eukaryotic viral genome is contained in the recombinant molecule?

D. Occupational Health and Safety

Discuss in detail below what procedures will be followed to assure proper protection of personnel.

D.1. Please state biosafety level work will be conducted at and include a justification for choosing this level.

Final containment levels are the decision of the IBC.

Insert text here

PI INITIALS: _____

D.2. Other safety considerations

Check	Hazard Category
	Radioisotopes (may require changes to radiation materials license)
	Chemical Hazards
	Controlled Substances
	Primary Human Tissue (requires BBP training)
	Other

D.3. Use as much space as necessary to fill in fields below.

Specific hazard	Hazard Category	Precautions

E. Personnel

Provide below the names, titles and training each person working under this protocol has received. Include number of years working with recombinant or synthetic nucleic acid molecules and specific details of experience. Use as much space as is necessary. A copy of each individual's CV must also be on file.

Employee Name	Role (Supervisor or Researcher)	Years of Experience with Material	CV on File (Y/N)

F. Location of Recombinant or Synthetic Nucleic Acid Molecules Use

Please list room numbers or names where work will take place.

Insert text here

G. Transfer of Materials

Will any of the materials be shipped between facilities? Please copy chart for each co-investigator.

Name:	
Address:	
Phone:	

APPENDIX VI: RETROVIRAL VECTORS

A retrovirus is an enveloped virus that uses RNA as its genetic material. Retroviruses replicate by inserting their RNA and an associated integrase and reverse transcriptase into the host cell. Once inside the cell, the virus uses its own reverse transcriptase to produce DNA from its RNA and this DNA is then incorporated into the cell's genome using the viral integrase. The cell then transcribes and translates the viral genes along with structural and enzymatic proteins (such as *gag*, *pol* and *env*) allowing the retrovirus to replicate. A retrovirus is in the family which includes the genera *Gammaretrovirus* and *Lentivirus* that are more typically used in research.

Retroviral vectors are vectors created from a retrovirus that has been modified to allow delivery of specific genetic material into target cells. Gammaretroviral vector systems are used to integrate transgenes into dividing cells. Lentiviral vector systems have the benefit of having the ability to integrate transgenes into dividing and non-dividing cells, making them more efficient and preferred by researchers. Most lentiviral vector systems are derived from the species Human Immunodeficiency Virus 1 (HIV-1) which is a Risk Group 3 organism. Lentiviruses are known to have high mutation and recombination rates which may lead to the potential of developing a replication competent virus or oncogenesis; therefore, modifications have been made to these vector systems to increase their safety and avoid the possibility of self-replication. Generally, guidelines recommend BSL-2 or BSL-2 enhanced practices for working with the lentiviral vector systems; however, a risk assessment should be performed to determine the appropriate containment level. The risk assessment should consider the nature of the vector system, transgene insert and host, the vector titer and amount, exposure potential, potential risk of insertional mutagenesis, and the containment level of the animal host (if relevant).

Lentiviral Vector Systems

Lentiviral vector systems are divided into different generations based on their features. The higher the generation number, the less likely a recombination or oncogenesis event will occur.

1. First-generation lentiviral vector systems contain a significant portion of the HIV genome except for the env gene which is located on a separate plasmid from the other lentiviral genes. Some systems pseudotype or replace the gene with vsv-g gene to enhance stability and tropism.

2. The second-generation lentiviral vector systems also have the env gene located on a separate plasmid and lack the accessory virulence factors vif, vpr, vpu and nef. The packaging plasmid contains gag, pol, tat and rev.

3. Third-generation lentiviral vector systems are the most commonly used and genes are separated into three plasmids making recombination events less likely. The tat gene is removed, the rev gene is placed on a separate plasmid and a deletion to the 3' long terminal repeat (LTR) end is introduced to make the virus self-inactivating (SIN) after integration. Virulence factors are all absent similar to second-generation vectors.

4. The fourth-generation lentiviral vectors have the tat gene, similar to the second-generation lentiviral vectors, but genes are separated into five plasmids to further

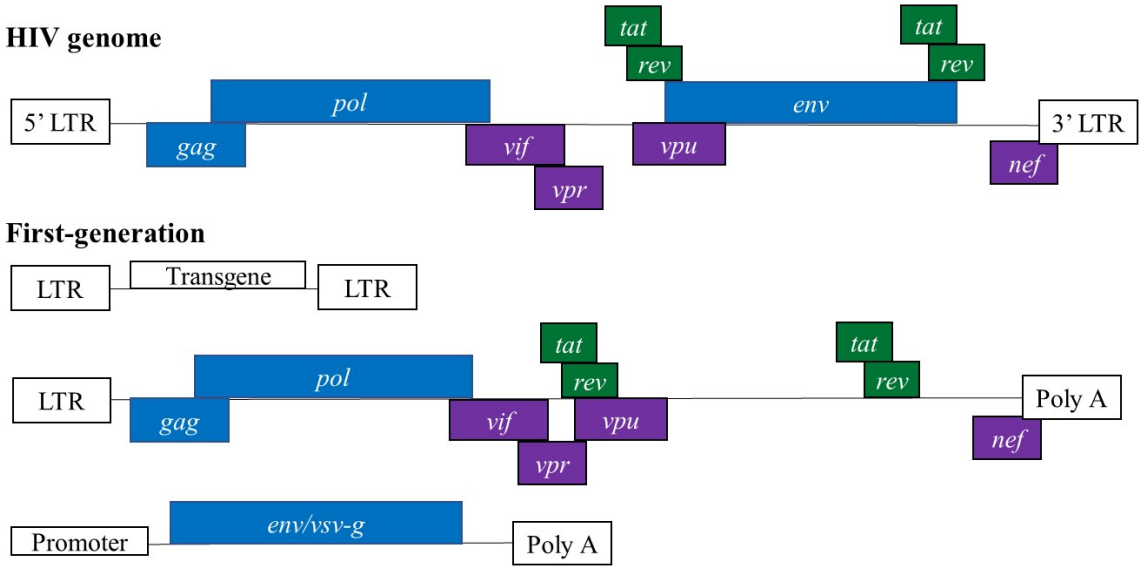
decrease the probability of recombination events. Fourth-generation vectors lack some virulence factors.

Even with the implementation of these modified lentiviral vector systems, replication competent or wild-type HIV storage or work should be avoided to prevent the potential creation of a replication competent virus. The safety risk is also increased when the gene expression results in the suppression of tumor suppressors or overexpression of oncogenes or proto-oncogenes.

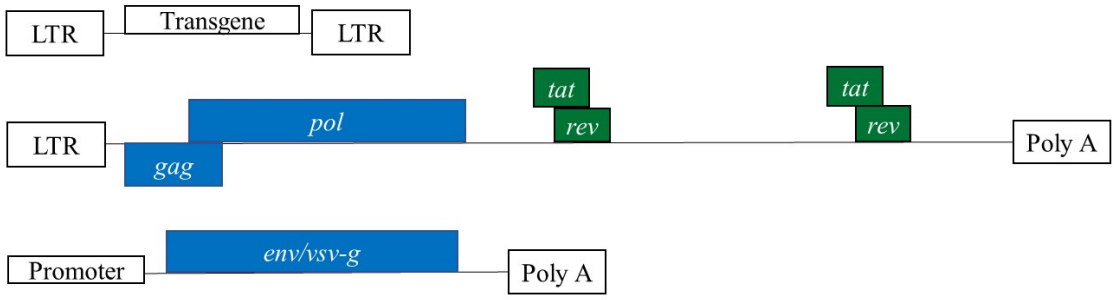
HIV Genome

	Gene		Protein
Structural Proteins	*gag*	group-specific antigen	core and matrix proteins
	pol	polymerase	codes for reverse transcriptase, RNase H, integrase and HIV protease
	env	envelope	codes the protein forming viral envelope
Regulatory Proteins	*tat*	transactivator	regulates reverse transcription of viral RNA
	rev	regulator of expression of viral proteins	involved in the export of unspliced and incompletely spliced mRNAs out of the nucleus for translation
Accessory Proteins	*vif*	viral infectivity	synthesizes infectious viruses for certain cell types
	vpr	viral protein R	imports DNA to nucleus, arrests cell cycle in G2 phase, may help integrate viral DNA into cell
	vpu	viral protein U	involved in CD4 degradation and release of virus from infected cells
	nef	negative regulation factor	involved in replication of the virus, enhances virus infectivity

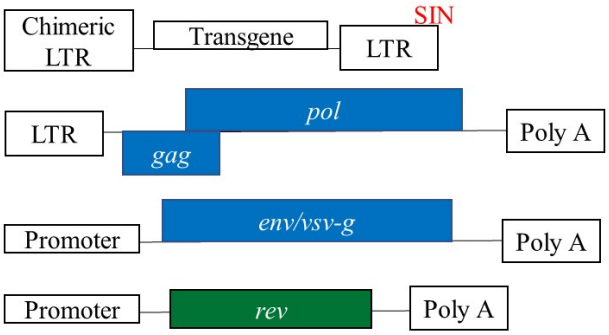
Diagrams of Lentiviral Vector Systems



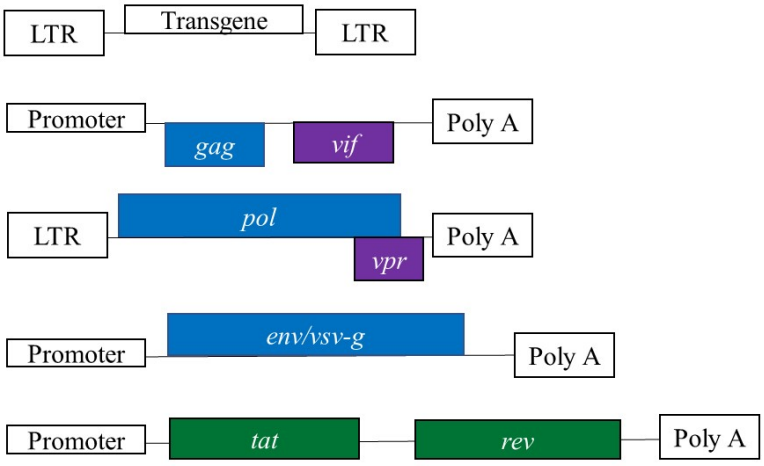
Second-generation



Third-generation



Fourth-generation



APPENDIX VII: WORKING WITH ADENO-ASSOCIATED VIRUS (AAV)

Adeno-Associated Virus (AAV) is a commonly used viral vector in the laboratory. It is a non-enveloped, single-stranded DNA virus, and a member of the Parvovirus family. The virus itself is not known to cause disease, but may elicit a mild immune response.

AAV can infect both dividing and non-dividing cells and is replication-deficient in the absence of helper virus, making it a useful tool in the laboratory. AAV generally has a broad tropism for many different cell types.

Biosafety Containment

AAV is a risk group 1 agent. As such, AAV and recombinant AAV (rAAV) can be used safely at BSL-1 after conducting a risk assessment and if *all* the following are true:

- Native AAV or rAAV made without helper virus (e.g., adenovirus, herpes simplex virus (HSV), or any helper virus of human origin)
- Not propagated in human cell lines (e.g., HEK 293 cells)
- Not coding for hazardous gene products (e.g., oncogenes, toxins, tumor suppressor inhibitors)

If any of the above are not true, then this work must be performed at BSL-2.

Hazards

Infection routes for AAV and rAAV include:

- Contact with mucous membranes
- Ingestion
- Injection or sharps injury

Infection with rAAV may result in the insertion of the gene of interest into the host genome in the presence of helper virus or wild type adenovirus in the host.

Controlling Exposure Risk

Work with AAV and rAAV that falls under BSL-2 should be performed in a biosafety cabinet (BSC). Avoid generating aerosols outside of the biosafety cabinet; when centrifuging, use bucket covers and open centrifuge tubes/bottles/plates inside the BSC, or let sit for at least 10 minutes before opening outside of the BSC to allow aerosols to settle.

Personal protective equipment (PPE) required while working with AAV and rAAV includes safety glasses, lab coat, and gloves.

Collect consumables (e.g., pipet tips, plates) used with virus inside the biosafety cabinet in a small red bag. Once the experiment is complete, the bag is sealed, and the outside is sprayed with 70% ethanol or 70% isopropanol before adding the bag to the biowaste container. Sharps use is discouraged, but when unavoidable, dispose of in a sharps container inside the BSC.

Regulated Waste

Consult Section 12 of this manual for more information.

Spill Response

Spill response is dependent on the biosafety level assigned to the work. Consult Section 17 of this manual for more information.

Exposure Response

Consult Section 16 of this manual for more information.

APPENDIX VIII: SELECT AGENTS LIST

The following biological agents and toxins have been determined to have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. An attenuated strain of a select agent or an inactive form of a select toxin may be excluded from the requirements of the Select Agent Regulations. The list of excluded agents and toxins can be found at: https://www.selectagents.gov/SelectAgentsandToxinsExclusions.html.

HHS and USDA Select Agents and Toxins
7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73

HHS Select Agents and Toxins

1. Abrin[6]
2. *Bacillus cereus* Biovar anthracis[1]
3. Botulinum neurotoxins[1,6]
4. Botulinum neurotoxin producing species of *Clostridium*[1]
5. Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence$X_1CCX_2PACGX_3X_4X_5X_6CX_7$)[6]
6. *Coxiella burnetii*
7. Crimean-Congo haemorrhagic fever virus
8. Diacetoxyscirpenol[6]
9. Eastern Equine Encephalitis virus[4,5]
10. Ebola virus[1]
11. *Francisella tularensis*[1]
12. Lassa fever virus
13. Lujo virus
14. Marburg virus[1]
15. Mpox virus[4,9]
16. Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)
17. Ricin[6]
18. *Rickettsia prowazekii*

Overlap Select Agents and Toxins

37. *Bacillus anthracis*[1]
38. *Bacillus anthracis* Pasteur strain
39. *Brucella abortus*
40. *Brucella melitensis*
41. *Brucella suis*
42. *Burkholderia mallei*[1]
43. *Burkholderia pseudomallei*[1]
44. Hendra virus
45. Nipah virus
46. Rift Valley fever virus
47. Venezuelan equine encephalitis virus[4,5,8]

USDA SELECT AGENTS AND TOXINS

48. African horse sickness virus
49. African swine fever virus
50. Avian influenza virus[4]
51. Classical swine fever virus[5]
52. Foot-and-mouth disease virus[1,5]
53. Goat pox virus
54. Lumpy skin disease virus
55. *Mycoplasma capricolum*[4]
56. *Mycoplasma mycoides*[4]

19. SARS-associated coronavirus (SARS-CoV)[5]
20. SARS-CoV/SARS-CoV-2 chimeric viruses resulting from any deliberate manipulation of SARS-CoV-2 to incorporate nucleic acids coding for SARS-CoV virulence factors
21. Saxitoxin[6]

South American Haemorrhagic Fever viruses:

22. Chapare
23. Guanarito
24. Junin
25. Machupo
26. Sabia
27. Staphylococcal enterotoxins (subtypes A,B,C,D,E)[6]
28. T-2 toxin[6]
29. Tetrodotoxin[6]

Tick-borne encephalitis complex (flavi) viruses:

30. Far Eastern subtype[5]
31. Siberian subtype[5]
32. Kyasanur Forest disease virus[5]
33. Omsk hemorrhagic fever virus[5]
34. Variola major virus (Smallpox virus)[1]
35. Variola minor virus (Alastrim)[1]
36. Yersinia pestis[1]
57. Newcastle disease virus[3,4]
58. Peste des petits ruminants virus
59. Rinderpest virus[1]
60. Sheep pox virus
61. Swine vesicular disease virus[5]

USDA PLANT PROTECTION AND QUARANTINE (PPQ) SELECT AGENTS AND TOXINS

62. *Coniothyrium glycines* (formerly *Phoma glycinicola* and *Pyrenochaeta glycines*)
63. *Peronosclerospora philippinensis* (*Peronosclerospora sacchari*)
64. *Ralstonia solanacearum*[7]
65. *Rathayibacter toxicus*
66. *Sclerophthora rayssiae*[7]
67. *Synchytrium endobioticum*
68. *Xanthomonas oryzae*

[1] Denotes Tier 1 Agent

[2] C = Cysteine residues are all present as disulfides, with the 1st and 3rd Cysteine, and the 2nd and 4th Cysteine forming specific disulfide bridges; The consensus sequence includes known toxins a-MI and a-GI (shown above) as well as a-GIA, Ac1.1a, a-CnIA, a-CnIB; X1 = any amino acid(s) or Des-X; X2 = Asparagine or Histidine; P = Proline; A = Alanine; G = Glycine; X3 = Arginine or Lysine; X4 = Asparagine, Histidine, Lysine, Arginine, Tyrosine, Phenylalanine or Tryptophan; X5 = Tyrosine, Phenylalanine, or Tryptophan; X6 = Serine, Threonine, Glutamate, Aspartate, Glutamine, or Asparagine; X7 = Any amino acid(s) or Des X and; “Des X” = “an amino acid does not have to be present at this position.” For example if a peptide sequence were XCCHPA then the related peptide CCHPA would be designated as Des-X.

[3] A virulent Newcastle disease virus (avian paramyxovirus serotype 1) has an intracerebral pathogenicity index in day-old chicks (Gallus gallus) of 0.7 or greater or has an amino acid sequence at the fusion (F) protein cleavage site that is consistent with virulent strains of Newcastle disease virus. A failure to detect a cleavage site that is consistent with virulent strains does not confirm the absence of a virulent virus.

[4] Select agents that meet any of the following criteria are excluded from the requirements of this part: Any low pathogenic strains of avian influenza virus, South American genotype of eastern equine encephalitis virus, west African clade of Mpox viruses, any strain of Newcastle disease virus which does not meet the criteria for virulent Newcastle disease virus, all subspecies *Mycoplasma capricolum* except subspecies capripneumoniae (contagious caprine pleuropneumonia), all subspecies *Mycoplasma mycoides* except subspecies mycoides small colony (Mmm SC) (contagious bovine pleuropneumonia), and any subtypes of Venezuelan equine encephalitis virus except for Subtypes IAB or IC, provided that the individual or entity can verify that the agent is within the exclusion category.

[5] For determining the regulatory status of nucleic acids that are capable of producing infectious forms of select agent viruses, please reference guidance here.

[6] For determining the regulatory status of Recombinant and/or Synthetic nucleic acids that encode for the toxic form(s) of any select toxins if the nucleic acids (i) can be expressed in vivo or in vitro, or (ii) are in a vector or recombinant host genome and can be expressed in vivo or in vitro; please reference guidance here.

[7] Select agents or toxins that meet any of the following criteria are excluded from the requirements of this part: Any subspecies of *Ralstonia solanacearum* except race 3, biovar 2 and all subspecies of *Sclerophthora rayssiae* except var. *zeae*, provided that the individual or entity can identify that the agent is within the exclusion category.

[8] Modified Venezuelan Equine Encephalitis Virus TC-83(A3G) strain is a select agent.

[9] Note that this is a change in nomenclature, which is aligned with the World Health Organization decision, and does not represent a change in the listed agent.

Reference: Select Agents and Toxins list, https://www.selectagents.gov/SelectAgentsandToxinsList.html, updated January 18, 2023.

APPENDIX IX: SCHEDULE OF CLEANING AND DECONTAMINATION

Below is the routine cleaning schedule for equipment used with bloodborne pathogens. As noted in the exposure control plan, all equipment is immediately cleaned after a spill occurs.

Equipment	Frequency	Disinfectant	Procedure
Incubators	Monthly	70% ethyl or isopropyl alcohol	Wipe down surfaces, autoclave shelves
BSC	Daily, as used	10% bleach (~0.5% sodium hypochlorite) followed by 70% ethyl or isopropyl alcohol	Wipe down surfaces. Lift grates and clean under work area as needed.
Biowaste lids	When boxes are closed for disposal	70% ethyl or isopropyl alcohol	Wipe all surfaces (top and underneath)
Centrifuges	Monthly	10% bleach (~0.5% sodium hypochlorite) followed by 70% ethyl or isopropyl alcohol	Wipe down surfaces, including centrifuge buckets and caps.

APPENDIX X: ANCILLARY PERSONNEL CAUTION

Ancillary personnel must wear PPE when entering the laboratories, following the requirements posted on door signage.

Ancillary personnel who enter the BSL-2 laboratory at AbCellera Boston must follow the guidelines below:

- Do not enter the BSL-2 laboratory unless all biowaste containers are closed and all materials are put away
- If a scientist is working, ask before entering
- Always wear PPE in the BSL-2 laboratory even if not required to do so in other laboratories or other companies

APPENDIX XI: SHARPS EVALUATION FORM

The federal Needlestick Safety and Prevention Act requires the investigation and use of sharps with engineered injury protections or needleless systems whenever possible. An example of this would be the use of a self-sheathing needle.

Input from researchers using sharps with human materials is required for the selection and use of safer medical devices. Complete the following initial survey form and return to the Biosafety Officer (BSO).

1. I work with human materials, or other potentially infectious materials (OPIM), such as blood, serum, tissue, bodily fluids, or human cell lines.	☐ Yes ☐ No
2. I use sharps, such as needles, razor blades, or scalpels in my work with human materials or OPIM.	☐ Yes ☐ No
If you answered no to question #2, skip the rest of the form, sign and return to the BSO.	
3. The tasks that involve the use of needles or sharps are (briefly describe):	
4. Have you seen devices on the market that may make your work safer or reduce the risk of sharps injury?	☐ Yes ☐ No
5. If yes, indicate the vendor and part number, as well as the vendor phone number or website link below.	
6. Are you interested in participating on an informal committee to select and evaluate sharps with engineered sharps injury protections and needleless systems when more become available to the market? *NOTE: If you come across a new engineered device that can be used in your work, bring it to the attention of the BSO for evaluation immediately.*	☐ Yes ☐ No

Print Name: _____ Department: _____

Signature: _____ Date: _____

APPENDIX XII: RECEIPT AND TRANSPORT OF BIOLOGICAL MATERIALS

Do not handle the package directly if the packaging looks compromised. If the package is damaged or leaking, put the package in a secondary container and call the Biological Safety Officer. Handle the package as a biological spill.

Transport all BSL-2 and above materials in a labeled, sealable, unbreakable secondary container. This can be a resealable bag, Tupperware™ type container, or biocarrier.

Packages of infectious or potentially infectious agents must be labeled with the universal biohazard symbol.

Regulated Material	Permit Application / Regulating Agency
Recombinant or Synthetic Nucleic Acid Molecules	Compliance with the NIH guidelines USDA PPQ 1001 if plant, animal or soil material is infective
Certain Human/Animal pathogens and all foreign human specimens (Receipt of human specimen from some areas is prohibited – Consult with the USDA/CDC as early as possible)	CDC 0.753 Centers for Disease Control and Prevention Biosafety Office 1600 Clifton Road, N.E. Atlanta, GA 30333 404-639-3883 https://www.cdc.gov/phpr/ipp/index.htm
Foreign animal cell cultures, foreign derived products, sera, hormones, milk, etc. Domestic pathogens and all foreign source material from animals, plants and soil. For information and advice:	USDA VS 16-3 + 7-R MA US Department of Agriculture Animal and Plant Inspection Service 10 Causeway Street Boston, MA 02222 617-565-7030 U.S. Department of Agriculture Animal and Plant Inspection Service 4700 River Road Riverdale, MD 20737 1-844-820-2234

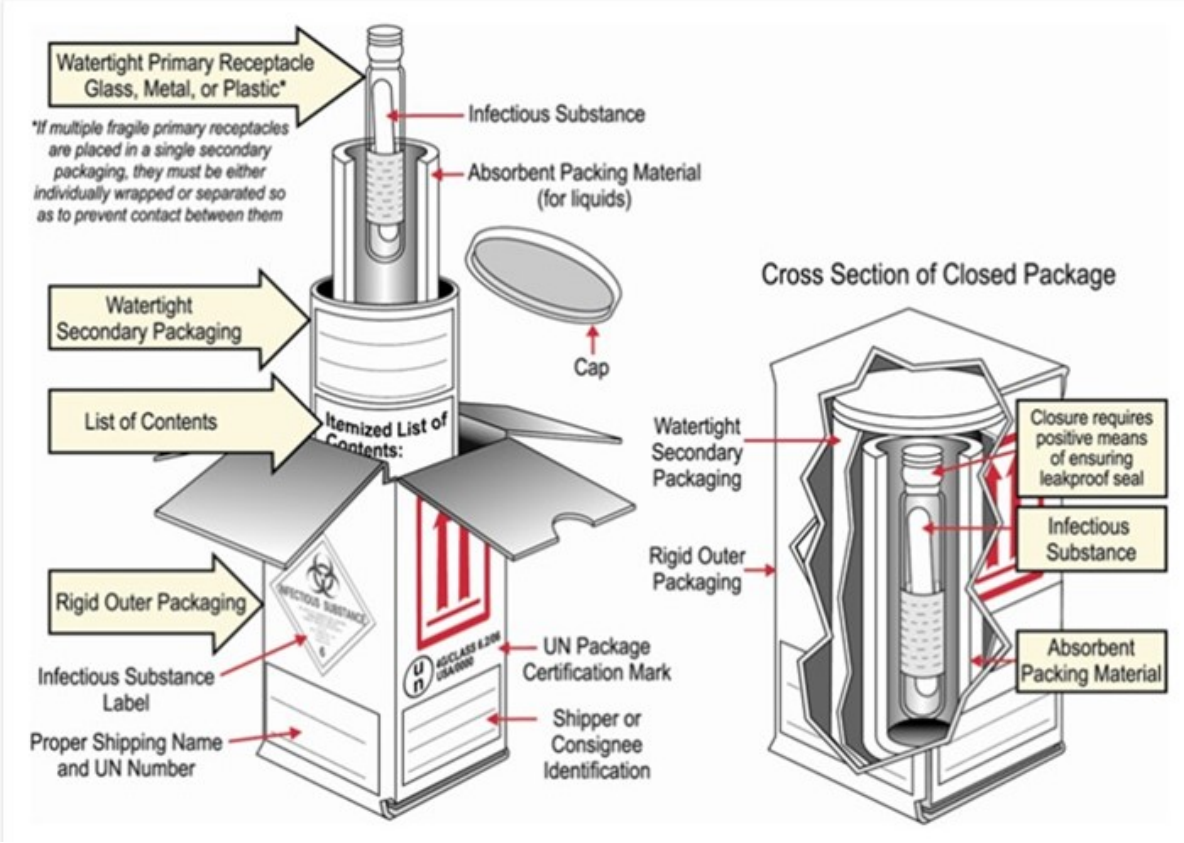
APPENDIX XIII: SHIPPING BIOHAZARDOUS SUBSTANCES

Department of Transportation (DOT) and International Air Transport Association (IATA) regulations must be followed for all shipments. Anyone who ships hazardous materials must be trained in DOT and IATA regulations.

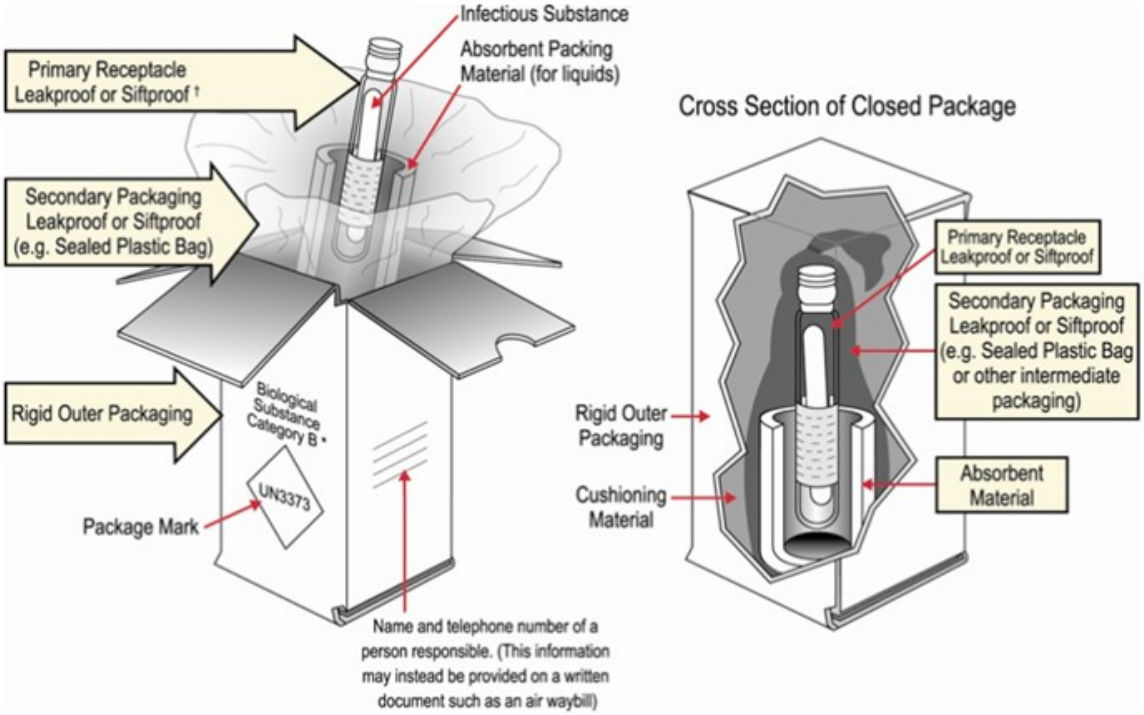
Packaging and labeling requirements for interstate shipment of infectious substances (etiologic agents) and clinical specimens.

Note that the shipper's name, address, and telephone number must be on the outer and inner containers. Refer also to additional provisions of the Department of Transportation (49 CFR Parts 171-180) Hazardous Materials Regulations.

Category A - Infectious Substance



Category B - Biological Substance



APPENDIX XIV: PERSONAL ELECTRONIC DEVICE USE IN THE LABORATORY POLICY

While they are useful and convenient tools, cell phones and other personal electronic devices can be a source of distraction and can potentially spread contamination if used carelessly in the laboratory. To ensure the safety of AbCellera Boston employees, the following safety guidelines regarding personal electronic devices must be followed in the laboratory.

Personal electronic devices must never be used directly with gloved hands. All employees must either remove their gloves and wash their hands each time before touching a personal electronic device in the lab, or the device must be placed into a zipper-closure bag prior to entering the laboratory and remain in the plastic bag until leaving the laboratory. When leaving the lab, the plastic bag must be disinfected before removing the phone.

Headphones may be used in the laboratory, provided the volume is kept low enough so that the scientist is aware of what is going on around him/her. Noise-cancelling headphones must never be used in the laboratory.

References:

Armstrong, J.A., and Froelich, E.J. 1964. Inactivation of viruses by benzalkonium chloride. Applied Microbiology, 12 (2): 132-137.

Fazlara, A., and Ekhtelat, M. 2012. The disinfectant effects of benzalkonium chloride on some important foodborne pathogens. American-Eurasian Journal of Agricultural & Environmental Science, 12 (1): 23-29.

McDonnell, G., and Russell, A.D. 1999. Antiseptics and disinfectants: activity, action, and resistance. Clinical Microbiology Reviews, 12 (1): 147-179.

Oxford, J.S., Potter, W., McLaren, C., and Hardy, W. 1971. Inactivation of influenza and other viruses by a mixture of virucidal compounds. American Society for Microbiology, 21 (4): 606-610.

APPENDIX XV: DISINFECTANTS

Summary of Practical Disinfectants

	Quaternary ammonium compounds	Phenolic compounds	Chlorine compounds	Iodophors	Ethyl alcohol	Isopropyl alcohol	Formaldehyde	Glutaraldehyde
Inactivates								
Vegetative bacteria	+	+	+	+	+	+	+	+
Lipoviruses	+	+	+	+	+	+	+	+
Nonlipid viruses	-	a	+	+	a	a	+	+
Bacterial spores	-	-	+	+	-	-	+	+
Treatment requirements								
Use dilution	0.1-2.0%	1.0-5.0%	500ppm[b]	25-1600 ppm[b]	70-85%	70-85%	0.2-8.0%	2%
Contact time (min)								
Lipoviruses	10	10	10	10	10	10	10	10
Broad spectrum	NE	NE	30	30	NE	NE	30	30
Important characteristics								
Effective shelf life >1 week [c]	+	+	-	+	+	+	+	+
Corrosive	-	+	+	+	-	-	-	-
Flammable	-	-	-	-	+	+	-	-
Explosive potential	-	-	-	-	-	-	-	-
Inactivated by organic matter	+	-	+	+	-	-	-	-
Skin irritant	+	+	+	+	-	-	+	+
Eye irritant	+	+	+	+	+	+	+	+
Respiratory irritant	-	-	+	-	-	-	-	-
Toxic [d]	+	+	+	+	+	+	+	+
Applicability								
Waste liquids	-	-	+	-	-	-	-	-
Dirty glassware	+	+	+	+	+	+	+	+
Equipment, surface decon.	+	+	+	+	+	+	+	+
Proprietary products [e]	CDQ End-Bac Hi-Tor Mikro-Quat	Hil-Phene Matar Mikro-Bac O-Syl	Chloramine T Clorox Purex	Hy-Sine Ioprep Mikroklene Wescodyne			Sterac	Cidex

+ = Yes; - = No; NE = Not effective
[a] Variable results depending on virus
[b] Available halogen
[c] Protected from light and air
[d] By skin or mouth or both. Refer to manufacturer's literature or Merck Index.

[e] Space limitations preclude listing all products available. Individual listings (or omissions) do not imply endorsement (or rejection) of any product by the National Institutes of Health or the U. S. Environmental Protection Agency.

Reference: Van Houten, J., 1989. New Frontiers in Biosafety: The Industrial Perspective. In Biohazard Management Handbook, Liberman, D.F. & Gordon, J.G. (Eds), pp.199-200, New York, Marcel Dekker, Inc.

Activity Levels of Selected Disinfectants

Class	Use-Concentration of Active Ingredient	Activity Level
Gas		
Ethylene oxide	450-500 mg/L*	High
Liquid		
Glutaraldehyde, aqueous**	2%	High
Formaldehyde + alcohol	8% + 70%	High
Stabilized hydrogen peroxide	6-10%	High
Formaldehyde, aqueous	3-8%	High to intermediate
Iodophors	30-50 mg/L free iodine 20-150 mg/L available iodine***	Intermediate
Iodine + alcohol	0.5% + 70%	Intermediate
Chlorine compounds	0.1 - 0.5% free chlorine	Intermediate
Phenolic compounds, aqueous	0.5 - 3%	Intermediate to low
Quaternary ammonium compounds	0.1 - 0.2% aqueous	Low
Mercurial compounds	0.1 - 0.2%	Low

* In autoclave-type equipment at 55° to 60° C.

** There are several proprietary formulations on the U.S. market, i.e., 4% glutaraldehyde and 3% formaldehyde; glutaraldehyde 2% and 7% buffered phenol; and glutaraldehyde 2%, low pH and normal and raised temperatures.

*** There are semantic problems associated with iodophors, available iodine, and free iodine.

Preparation and Stability of Chlorine Solutions

	Desired Chlorine concentration			
	5000 ppm	**1000 ppm**	**500 ppm**	**100 ppm**
Dilution of bleach (5% NaOCl) Prepared fresh for use within 24 hr	1:10*	1:50	1:100	1:500
Dilution of bleach (5% NaOCl) Prepared fresh and used for 1-3 days	1:5†	1:25	1:50	1:250

* To achieve a 1:10 dilution, add one part regular strength bleach to nine parts water.

† To achieve a 1:5 dilution, add one part regular strength bleach to four parts water.

Reference: Rutala, W.A., APIC Guidelines for selection and use of disinfectants, Am J Infect Control, 24:326,1996.

Inactivation of HBV And HIV By Disinfectants

Disinfectant	Concentration inactivating 10^8 HBV in ST, 10 min, 20° C*	Concentration inactivating 10^5 HIV in ST, ≤ 10 min, 25° C†
Ethyl alcohol	ND	50%
Glutaraldehyde	2%	ND‡
Glutaraldehyde-phenate	0.13% glutaraldehyde 0.44% phenate	ND
Hydrogen peroxide	ND	0.3%
Iodophor	80 ppm	ND
Isopropyl alcohol	70%	35%
Paraformaldehyde	ND	0.5%
Phenolic	ND	0.5%
Sodium hypochlorite	500 ppm	50 ppm

ST - Suspension test

ND - No data

* Data from Bond *et al*.

† Data from Martin *et al*. Also see Sattar and Springthorpe for data concerning activity of other disinfectants HIV.

Reference: APIC Guidelines for Selection and Use of Disinfectants, Rutala, W.A., Am J Infect Control. 24:322,1996.

APPENDIX XVI: AUTOCLAVE SAFETY

Every autoclave is different, so refer to the operator's manual for specific instructions on operation of the autoclave.

Procedure

There are several practices that will minimize the chance of a serious accident occurring, but also increases the functionality of the autoclave.

- Before using the autoclave, check to make sure no items were left inside by the previous user that could pose a hazard.
- Clean the drain strainer before loading the autoclave.
- Load the autoclave properly as per manufacturer's recommendations.
    - Before loading containers of liquids into the autoclave, the caps must be loosened to avoid having the bottles shatter during pressurization.
    - Individual glassware pieces should be in heat resistant plastic trays on a shelf or rack and never placed directly on the autoclave bottom or floor.
    - Use a tray with a solid bottom and walls to contain the contents and catch spills.
    - Add ¼ to ½ inch of water to the tray so the bottles will heat evenly.
    - Make sure plastic materials are compatible with being autoclaved.
- Make sure the autoclave door is fully closed and latched and the correct cycle is selected before starting the cycle.
- Wear heat resistant gloves when operating the autoclave door after a cycle.
- If the door must be opened prior to the "cool down" cycle being completed, stand behind door when opening and beware rush of steam. Be sure to wear eye and face protection.
    - For non-liquid glassware loads allow the material to cool for 15 minutes prior to touching it with ungloved hands. If the material is waste wear at least latex or equivalent gloves to place the waste in the proper medical waste container.
    - For liquid loads allow the material to cool for one (1) hour before touching with ungloved hands. Inform others in the area that a heat hazard is present.
- When removing items from the autoclave, wear heat resistant gloves. A rubber apron is also recommended.

Prohibited Autoclave Activities

NEVER put solvents, volatile or corrosive chemicals (such as phenol, chloroform, bleach, etc.) or radioactive materials in an autoclave. Contact the Chemical Hygiene Officer if you have questions about proper disposal of these materials.

APPENDIX XVII: BLOODBORNE PATHOGENS TRAINING REQUIREMENTS

AbCellera Boston has established a mandatory Bloodborne Pathogens training program for all employees with occupational exposure. AbCellera Boston trains each affected employee in accordance with the requirements in the Bloodborne Pathogens Standard (29 CFR 1910.1030) section (g)(2). This training is provided at no cost to employees and during regular working hours.

Frequency of Training

Training is provided:

- At the time of initial assignment to tasks where occupational exposure may take place
- At least annually thereafter
    - Annual training for all employees shall be provided within one year of their previous training
- When changes (such as modification of tasks or procedures or institution of new tasks or procedures) affect the employee's occupational exposure
    - The additional training may be limited to addressing the new exposures created

Training Content

Training contains content applicable to the work employees are performing and is appropriate to the educational level, and language of employees.

The training program contains the following elements:

- An accessible copy of the regulatory text of the OSHA Bloodborne Pathogens Standard and an explanation of its contents
- A general explanation of the epidemiology and symptoms of bloodborne diseases
- An explanation of the modes of transmission of bloodborne pathogens
- An explanation of the employer's Exposure Control Plan and the means by which the employee can obtain a copy of the written plan
- An explanation of the appropriate methods for recognizing tasks and other activities that may involve exposure to human blood and other potentially infectious materials

- An explanation of the use and limitations of methods that will prevent or reduce exposure including appropriate engineering controls, work practices, and personal protective equipment
- Information on the types, proper use, location, removal, handling, decontamination, and disposal of personal protective equipment
- An explanation of the basis for selection of personal protective equipment
- Information on the hepatitis B vaccine, including information on its efficacy, safety, method of administration, the benefits of being vaccinated, and that the vaccine and vaccination will be offered free of charge
- Information on the appropriate actions to take and persons to contact in an emergency involving blood or other potentially infectious materials
- An explanation of the procedure to follow if an exposure incident occurs, including the method of reporting the incident and the medical follow-up that will be made available
- Information on the post-exposure evaluation and follow-up that the employer is required to provide for the employee following an exposure incident
- An explanation of the signs and labels and/or color coding required by the Bloodborne Pathogens Standard
- An opportunity for interactive questions and answers with the person conducting the training session

The person conducting the training shall be knowledgeable in the subject matter covered by the elements contained in the training program as it relates to the workplace that the training will address.

APPENDIX XVIII: SHARPS INJURY LOG

OSHA's Bloodborne Pathogens Standard requires employers to establish and maintain a Sharps Injury Log for recording all percutaneous injuries in a facility occurring from contaminated sharps. The purpose of the Log is to aid in the evaluation of devices being used in healthcare and other facilities and to identify problem devices or procedures requiring additional attention or review. This log must be kept in addition to the incident report.

The Sharps Injury Log should include all sharps injuries occurring in a calendar year. The log must be retained for five years following the end of the year to which it relates. The Log must be kept in a manner that preserves the confidentiality of the affected employee.

Date	**Case / Report Number**	**Type of Device** (e.g., syringe, suture needle)	**Brand Name of Device**	**Work Area where injury occurred** (e.g., TC lab, Biology lab)	**Brief description of how the incident occurred** (i.e. procedure being done, action being performed (disposal, injection, etc.), body part injured)

APPENDIX XIX: HEPATITIS B VACCINATION

The OSHA Bloodborne Pathogens Standard, 29 CFR 1910.1030, requires that the hepatitis B vaccination be made available to all employees who are occupationally exposed to human source materials including blood, serum, plasma and all other potentially infectious materials (OPIM). The vaccine is offered after the employee has received bloodborne pathogens (BBP) training as required by the standard and within 10 working days of initial assignment. Vaccination is encouraged unless:

- The employee has already had the hepatitis B vaccination series
- Antibody testing has revealed that the employee is immune
- The vaccine is contraindicated for medical reasons

The employee is given the option to accept or decline the vaccination after being told of the benefits and risks of the vaccine during BBP training

The availability of the Hepatitis B vaccine is part of the company's compliance to the BBP Standard, which also includes:

- An exposure control plan
- New employee and annual training
- A safer sharps program
- A sharps injury log

The attached hepatitis B vaccine form must be completed by all employees during bloodborne pathogens training. If the hepatitis B vaccine is declined initially, the employee can choose to receive it at any time during employment at no cost to them, including post-exposure, change of assignment, or at any other time while still covered under the Bloodborne Pathogens Standard.

Hepatitis B Vaccination Form

I understand that due to my occupational exposure to blood or other potentially infectious materials I may be at risk of acquiring a hepatitis B virus (HBV) infection. I have been given the opportunity to be vaccinated with the hepatitis B vaccine, at no charge to myself.

Please complete **one** of the following boxes:

If you do not wish to obtain the hepatitis B vaccine OR have already been immunized and do not wish to have a titer taken:

Check one:

☐ DECLINATION: I decline hepatitis B vaccination at this time. I understand that by declining this vaccine I continue to be at risk of acquiring hepatitis B, a serious disease. If, in the future I continue to have occupational exposure to blood or other potentially infectious materials and I want to be vaccinated with hepatitis B vaccine, I can receive the vaccination series at no charge to me.

-OR-

☐ STATEMENT OF PREVIOUS IMMUNIZATION: I attest that I have previously been immunized against hepatitis B virus (HBV) infection.

Print Name _____ Signature _____ Date _____

If you have not been previously immunized and would like to obtain the hepatitis B vaccine:

☐ CONSENT FOR VACCINE AND TITER: I understand the risks and benefits of the hepatitis B vaccine and that I will need to receive a series of three shots followed by a scheduled titer to complete the vaccine. I would like to participate in the hepatitis B vaccination program as offered by AbCellera Boston. The vaccination series and titer are offered at no cost to me. I agree to go to Mt. Auburn Occupational Health, located at 725 Concord Ave, Suite 5100, Cambridge to participate in this program.

Print Name _____ Signature _____ Date _____

If you have been previously immunized and would like to ensure you are still immune:

☐ REQUEST FOR TITER: I have previously received the hepatitis B vaccination, but I would like to have my titer evaluated and a booster administered if necessary.

Print Name _____ Signature _____ Date _____

APPENDIX XX: REFERENCES

Biosafety in the Microbiological and Biomedical Laboratory, https://www.cdc.gov/labs/BMBL.html, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Institutes of Health, Sixth Edition, June 2020, US Government Printing Office, Washington: 2020

Fleming, Diane O. and Debra L. Hunt, Biological Safety Principles and Practices, Third Edition, ASM Press, Washington, D.C., 2000

Laboratory Biosafety Guidelines, Third Edition, Minister of Health, Public Health Agency of Canada, Center for Emergency Preparedness and Response, 2004

OSHA Bloodborne Pathogens Standard, 29 CFR 1910.1030, https://www.osha.gov/laws-regs/regulations/standardnumber/1910/1910.1030

OSHA Bloodborne Pathogen Interpretation Letter, June 21, 1994

OSHA Ethylene Oxide Fact Sheet

American Biological Safety Association, https://www.absa.org/

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, https://osp.od.nih.gov/biotechnology/nih-guidelines/, Department of Health and Human Services, National Institutes of Health, April 2019

Safety Considerations for Retroviral Vectors: A Short Review, Prepared by Donald E. Mosier, TSRI Institutional Biosafety Committee Chair with the assistance of Carolyn Keierleber, TSRI Biosafety Officer and Associate Director of Environmental Health & Safety and Richard Gulizia, TSRI BSL-3 Facility Director

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JOB SAFETY ANALYSIS (JSA) FORM

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Department: Genetics

Date: June 9, 2023

Supervisor: Janna Bednenko

Task Name: Use of Cadmium Chloride for Large Culture Production

Lab/Room Number Where Task is Performed: Main BSL-1 lab

JSA Conducted by: Joanna Proctor

Break down the task into approximately 10 steps, but use more if necessary. Be as specific as possible about what material is used, where the steps are done and how it is done.

Task/Step	Potential Hazard(s) if any	Recommended Control(s)
1. Growth of Tetrahymena in WAVE25 – up to 25L culture in BSL-1 lab.	Spills	Have spill tray as secondary containment under WAVE25.
2. Preparation of Cadmium chloride concentrate solution: measure 50 g of Cadmium and dissolving in 50 ml distilled water.	Cadmium chloride powder inhalation, skin and eye contact. Spill of cadmium concentrate solution.	Cadmium chloride solution is made inside of fume hood PPE (Buttoned lab coat, safety glasses, gloves)
3. Induction of Tetrahymena by injection of a cadmium chloride concentrate solution (2 g/L) into WAVE25 in BSL-1 lab	Cadmium chloride concentrate (1 g/mL) and/or dilution (2 mg/L); exposure (skin and eye contact); spills	Have a spill tray as secondary containment under WAVE25. PPE (Buttoned lab coat, safety glasses, gloves)
4. Incubation of Tetrahymena with cadmium chloride for 6.5-16 h in WAVE25 in BSL-1 lab.	Cadmium chloride 2 mg/L; Spills	Have a spill tray as secondary containment under WAVE25
5. Harvest of Tetrahymena by taking 1L aliquots from the WAVE25 and	Cadmium chloride 2 mg/L; exposure (skin and eye contact; aerosols	Have a spill tray as secondary containment under WAVE25

spinning them down in LYNX6000 centrifuges.	from centrifuging); spills	When pouring liquids, use of a funnel to reduce spill risk PPE (Buttoned lab coat, safety glasses, gloves)
6. Disposing WAVE25 bags and liquid into segregated waste containers.	Cadmium chloride 2 mg/L; exposure (skin and eye contact, aerosols from waste pouring); spills	Labelled waste containers for cadmium chloride material only, stored in a secure waste room separated from the BSL-1 lab. PPE when handling waste When pouring liquids, use of a funnel to reduce risk of spills

Other Comments: Calcium chloride is toxic, carcinogenic, and a reproductive toxin. It can also cause target organ effects.

Additional Recommendations:

These include using a fume hood when preparing the cadmium chloride solution. This is often done by laying down a spill pad in the fume hood and working over. The Cadmium is stored in a secure location.

JSA Approved by: (client) **Signature:** **Date:**

AbCellera Boston Institutional Biosafety Committee (IBC) Meeting Minutes

Date: December 21, 2022
Time: 4:00 PM – 5:00 PM
Location: Remote Zoom meeting

All members in attendance: Joanna Cardarelli, Project Manager, IBC Chairperson and Biosafety Officer; Paul Colussi, Senior Vice President, Research; Janna Bednenko, Head of Protein Expression and Genetics; Sarah Augood, Community Representative (Arlington); Bonnie Weeks, Community Representative (Arlington); Beth Graham, Safety Consultant (non-voting member)

1. Welcome and Introductions of Members
    - All members were welcomed and the Community Representatives were thanked for their participation

2. Overview of an IBC (presentation by Beth)
    - General background on IBCs and the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules was provided
    - Requirements for IBC meeting frequency were reviewed
    - IBC membership requirements were presented
    - The purpose of an IBC was explained
    - The role of IBC members was discussed
    - AbCellera Boston's IBC is registered with the NIH Office of Science Policy (OSP)
    - Requirements of the Arlington Biosafety and Recombinant DNA Regulations were reviewed
        - An annual report must be sent with any changes in IBC membership, biosafety officer designation, management personnel, or any changes to the documentation submitted in initial application

3. Company and Scientific Review (presentation by Paul)
    - Background information on the company was presented
        - TetraGenetics was founded in 2004 by Cornell University faculty member
        - In September, 2021 TetraGenetics became a fully owned subsidiary of AbCellera Biologics
        - Company name was officially changed to AbCellera Boston in December, 2022
        - AbCellera is headquartered in Vancouver, BC, Canada and has 350+ employees
        - The AbCellera Executive Team and the AbCellera Boston Management Team (Paul Colussi, Vice President & Site Head) were reviewed
        - A map showing AbCellera's locations was presented: Vancouver, BC; Montreal, Que; Boston, MA; Cambridge, UK; Sydney AUS

- AbCellera Boston works closely with Vancouver (drug discovery) and Sydney
- Mission is still to develop the ciliated protist *Tetrahymena thermophila* as an expression host for the production of recombinant proteins for the discovery and development of therapeutic molecules
- Proprietary technology (TetraExpress™) developed by AbCellera Boston to generate recombinant human proteins for drug discovery programs
- Focus is complex membrane technologies
- Drug discovery efforts focus on targeting a subset of human proteins called ion channels that are implicated in many human diseases (e.g., autoimmune and pain); may branch out to produce other difficult to produce proteins
- Lab operations continue to be performed using Biosafety Level 1 (BSL1) and Biosafety Level 2 (BSL2) containment
- Background on *Tetrahymena thermophila* was provided
- The general work plan remains the same and involves: the cloning of a chemically synthesized gene of interest obtained from the same commercial vendor into *Tetrahymena* expression vectors; the introduction of expression vectors using biolistic transformation (aka gene gun); the selection of transformants in culture medium with antibiotic; the screening of clones for protein expression using an appropriate assay; currently scale-up to 6 liters (of the selected clones) with larger volumes planned for 2023; induction of gene expression with cadmium chloride; and breakup of the cell culture using a micro fluidizer to obtain the desired protein. The human protein of interest is then purified from cell lysates primarily using an AKTA to automate purification. Purified ion channel proteins are then formulated for drug discovery campaigns.
- None of the drug discovery is done in house; this is now done through AbCellera's Vancouver location
- The in-house characterization of drug candidates was described:
  - Drug candidates are screened and tested on mammalian cell lines (generally HEK293 and CHO); PBMCs are also used.
  - Screening capabilities include: FACS analysis, specific mammalian cell assays, and most frequently electrophysiology; electrophysiology is the most sophisticated system to measure electrical current and is the gold standard for looking at ion channels and detecting electrical currents.

4. **Safety Summary**
   - Biosafety program (presentation by Joanna)

- BSL1 appropriate for work involving *Tetrahymena thermophila* and *E. coli* which are not associated with disease in healthy adult humans: Risk Group 1
  - Minimal personnel and environmental risk
- BSL2 appropriate for work with PBMCs and established mammalian cell lines (CHO and HEK293)
  - Agents that can cause human disease, but effective prophylaxis/treatment generally available; limited environmental risk
- The Biosafety Manual & Exposure Control Plan was updated in April 2018 to include BL2 requirements
- The biosafety program was described including requirements for: a biosafety cabinet for BL2 work; personal protective equipment (PPE), safe work practices, safety training, occupational health, and emergency response procedures
- Changes related to the BL2 work include a requirement for annual bloodborne pathogens training and offering the Hepatitis B vaccine to all lab employees with potential exposure to bloodborne pathogens. There are also additional PPE requirements for the BL2 work that require lab coat, gloves, and safety glasses for all work.
- The three biological waste streams generated were reviewed
  - Liquid, Dry/Solid Waste, Sharps (Joanna noted that no needles are used, but sharps waste includes glass slides and blades)
- Liquid waste (e.g., cultures of *Tetrahymena*) is disinfected with freshly prepared 10% bleach (30 minute contact time) prior to sink disposal; cultures with cadmium are collected as hazardous waste.
- Veolia has been contracted to dispose of the solid biological waste, including sharps, which is stored in a designated posted waste room. Veolia also disposes of cultures containing cadmium (collected in 55 gallon drums) as hazardous waste.
- The safety-related permits held were reviewed; the rDNA permit renewal was just submitted; the company name on the permits is being changed

Joanna asked if there were any questions related to the safety program; there were no questions.

5. **2023 Research & Biosafety Updates**
   - The plans to bring in a WAVE-25 bioreactor were reviewed.
     - The work will be considered “large-scale” per the NIH Guidelines and Arlington BOH
     - The Wave bag will increase the amount of Tetrahymena growth to 25 liters at a time
     - Only oxygen tanks and compressed air are required

  - IBC approval submitted to the BOH is needed to begin work; a presentation to the BOH will also be required

- CryoEM Preparation will also begin in 2023
  - Will bring in the ability to make in-house grids for negative staining
  - Work will require the purchase of 1 mg of uranyl acetate
  - Chemical Hygiene Plan will be amended
  - Amount of uranyl acetate is exempt from requirement for a radiation license

AbCellera Boston IBC members responded to questions from the Community Representatives about the proposed 2023 work:

- *Will the large scale work change the NIH classification on the project registration?* Yes, the large scale work changes the classification to III-D. (Beth will provide AbCellera Boston with the complete definition of what work is included under III-D from the NIH Guidelines).
- *How many Wave bags will be used?* The plan is to get 2 wave bags.
- *Will the Wave bags be in containment?* The are not contained, but are made of durable plastic. There are no floor drains in the lab. Containment options were discussed such as spill decks with bladders to put underneath the Wave bags and rubberized berms. A Community Member also mentioned the importance of having pig socks on hand for spill containment. Beth noted that Veolia would be called to respond in the event of a large scale spill.
- *Will employees be trained on uranyl formate work?* Yes, the Chemical Hygiene Plan is being updated to include an appendix on uranyl formate safety which employees will be trained on.

6. **Project Registration and Waste Management Practices Review and Approval**

- Project 001-2011 Heterologous Protein Expression from *Tetrahymena thermophila*

  The project registration was reviewed by Paul and Janna. Changes included the addition of proposed large scale work (Section C4) and updates to Section E (Personnel). It was noted by IBC members that the NIH classification should be updated (Section A); uranyl acetate should be added (Section D 3), and the strain of E. coli being used should be included (Section C3). These changes were made to the project registration following the IBC meeting.

AbCellera Boston IBC members responded to questions from the Community Representatives about the project registration:

- *Will the amount of Tetrodotoxin used increase as a result of the large scale work?* No, the amount used will not increase.

- *What strain of E. coli is used?* A non-pathogenic strain of E. coli is used. It was confirmed following the meeting that all E. coli is strain K-12.
- *What material is being shipped between facilities?* Usually just proteins are shipped, but occasionally cell lines are shipped. No rDNA material is currently shipped between sites, but it's possible it could be in the future. (The statement in Section G was made more general following the meeting to read "Small quantities of materials may be shipped to collaborators for additional testing.)

There were no further questions.

- Beth asked if anyone would like to make a motion to approve this project
  - Sarah made a motion to approve the project
  - Bonnie seconded the motion
- Beth asked that all who approve the project registration for one year raise their hand
  - All in attendance raised their hands. **Project 001-2011 (including the large scale work) was approved.**

- Beth asked if there were any questions regarding biological waste management practices. There were no further questions.
  - Beth asked if anyone would like to make a motion to approve the waste management practices
    - Bonnie made a motion to approve
    - Sarah seconded the motion
  - Beth asked that all who approve the waste management practices raise their hand
    - All in attendance raised their hands. **Biological waste management practices were approved.**

The Community Representatives were thanked for their participation. The meeting adjourned at 4:56 PM.

AbCellera Boston Institutional Biosafety Committee (IBC) Meeting Minutes

This written consent shall be filed with the records of the Institutional Biosafety Committee meetings.

Name	Signature	Date
Joanna Proctor	_____Joanna Proctor_____	01/09/2023_____
Paul Colussi	_____ _____	__01/23/2023_____
Janna Bednenko	_____ _____	__01/07/2023___
Sarah Augood	_____	_____
Bonnie Weeks	_____	_____
Beth Graham	_____	_____

2022 IBC MEETING

AbCellera Boston

Joanna Proctor, MsC
Beth Graham, consultant
Paul Colussi, PhD

YYYY-MM-DD

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OVERVIEW

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01 WHAT IS AN IBC?

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WHAT IS AN IBC?

- **A group established under the NIH Guidelines to provide local review and oversight of research involving Recombinant or Synthetic Nucleic Acid Molecules.**

- **TetraGenetics' IBC is registered with the NIH Office of Science Policy (OSP).**

- **Required by the Arlington Biosafety and Recombinant DNA Regulations.**

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WHAT IS THE PURPOSE OF AN IBC?

- **To provide local review and oversight of rDNA research**
- **To ensure adequate containment of biological agents in use**
- **To inform the public about experimental plans and protocols**
- **To communicate with Arlington Board of Health (BOH)**
  - ✓Minutes must be sent to the Arlington BOH.
  - ✓An annual report must also be sent with any changes in IBC membership, biosafety officer designation, management personnel or any changes to the documentation submitted in initial application

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IBC MEMBERSHIP

IBC membership must include at least 5 members :

•Two community representatives (at least one Arlington resident)

•Persons with expertise in DNA, biological safety and physical containment

•Persons knowledgeable in institutional commitments, policies, laws, standards, community issues, etc.

•A member of the laboratory technical staff

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WHEN IS AN IBC NEEDED?

IBC meetings must be held:

- Initial- prior to the initiation of research (2011)
- Significant change to an existing project registration (e.g., protocol, new technology, change in biosafety containment level)
- Introduction of new project registration
- Annually

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ROLE OF IBC MEMBERS

The role of IBC members includes:

Review experimental rDNA protocols to:

- Evaluate the expertise of the Principal Investigator (PI) and laboratory staff to conduct the work
- Evaluate the potential hazards of the work
- Evaluate the biological containment plan and facilities
- Evaluate if additional health surveillance of laboratory staff is needed
- Approve/disapprove project registrations

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OTHER REQUIREMENTS OF ARLINGTON BOH

Other requirements of Arlington BOH Regulations:

- Submit a Plan Review Packet (application) for the use of Biological Agents and/or rDNA within the Town of Arlington (April, 2015)
- Present to the Arlington BOH at Board meeting (May, 2015; April 2018 for permit amendment)
- Walkthrough by the Arlington BOH (December, 2015; August, 2018 for permit amendment)
- Formal approval of one of the Community Representatives by the Arlington BOH at Board Meeting (February, 2016)
- Renew permit on an annual basis

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02 COMPANY OVERVIEW

ABCELLERA BOSTON COMPANY OVERVIEW

TetraGenetics Inc.

Founded in 2004
Founded by a Cornell University faculty member-Prof Ted Clark
September 10, 2021: Became wholly owned subsidiary of AbCellera Biologics
Officially changed to AbCellera Boston in December 2022

AbCellera Biologics

Headquartered in Vancouver, BC, Canada
350+ employees

AbCellera Executive Team

Carl Hansen PhD, CEO, interim CTO
Veronique Lecault PhD, COO & Director
Tryn Stimart JD, CLO, CCO
Andrew Booth MBA, CFO

AbCellera Boston Management Team

Paul Colussi, PhD: Vice President & Site Head, CMPT

Mission

Develop the ciliated protist *Tetrahymena thermophila* as an expression host for the production of recombinant proteins for the discovery or development of therapeutic molecules.

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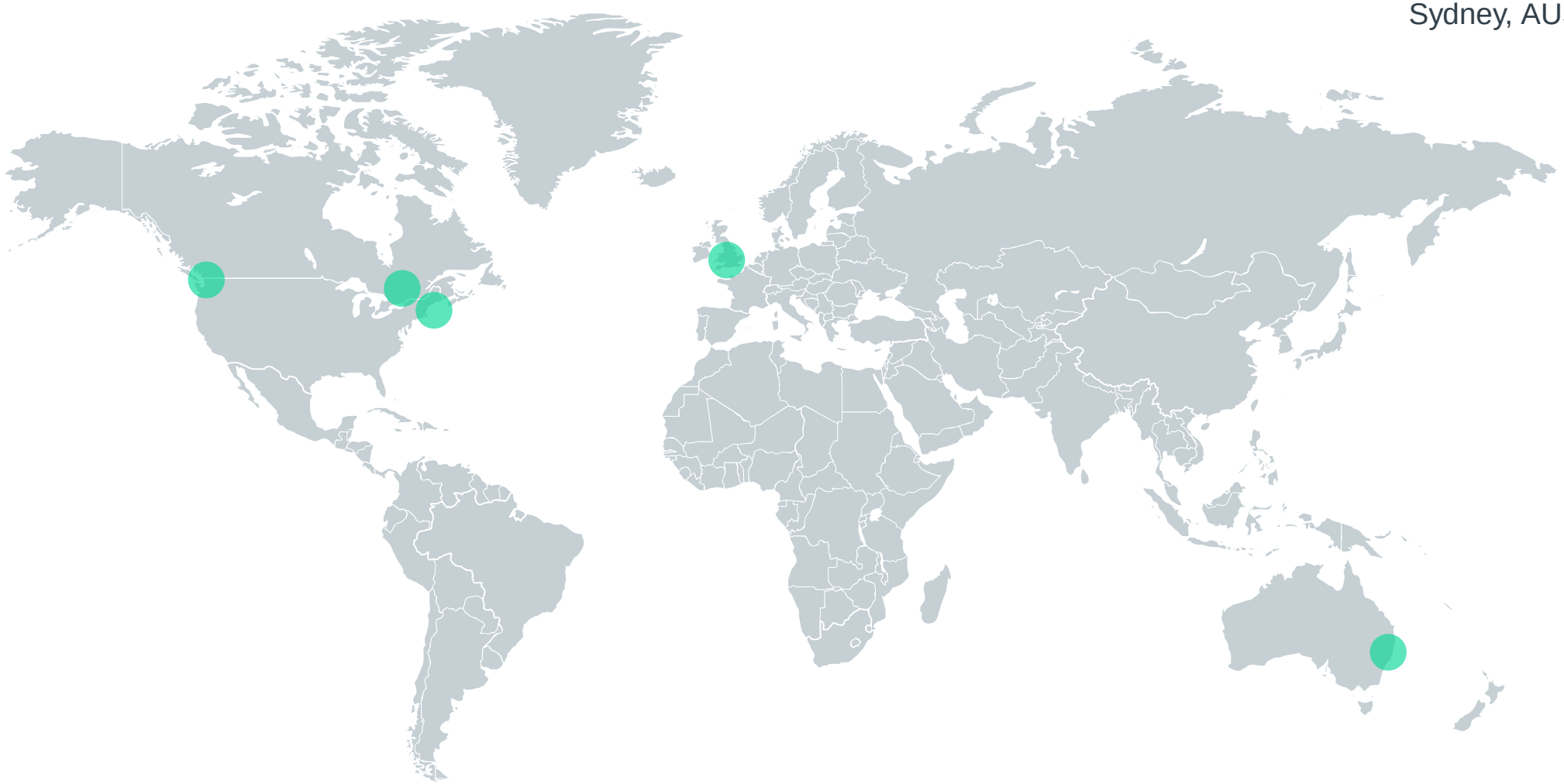
ABCELLERA LOCATIONS

Vancouver, BC
Montreal
Boston, MA
Cambridge, UK
Sydney, AUS



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RESEARCH ACTIVITIES: OVERVIEW

AbCellera Boston's focus is complex membrane technologies

Proprietary technology (TetraExpress™) developed by Abcellera Boston was developed to generate recombinant human proteins for drug discovery programs

Drug Discovery efforts focus on targeting a subset of human proteins called ion channels that are implicated in many human diseases e.g.

- Autoimmune
- Pain

Lab operations to date have occurred under Biosafety Level 1 (BL1) and Biosafety Level 2 (BL2)

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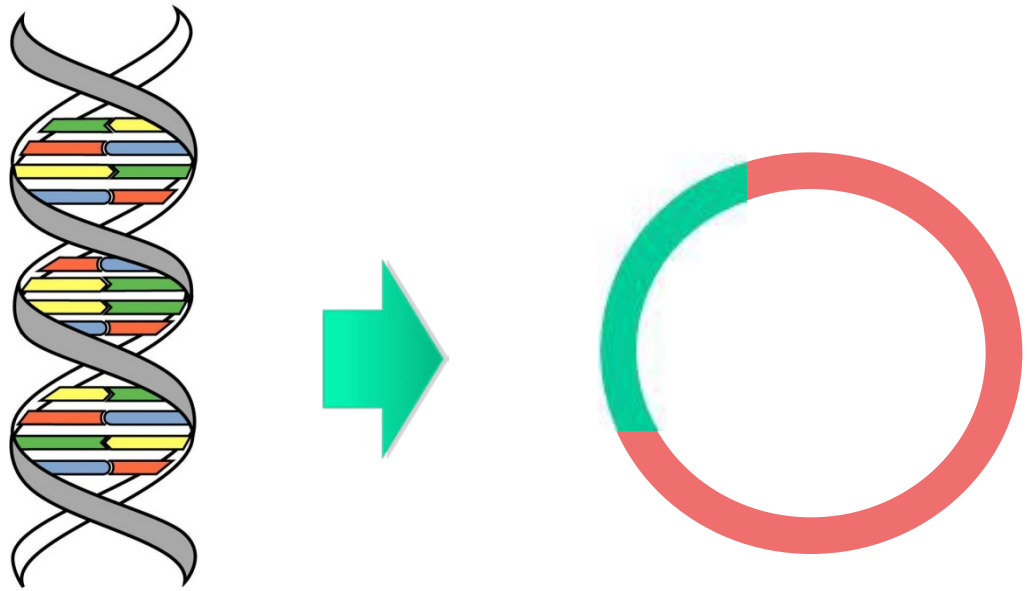
GENERALIZED WORK PLAN

Synthesize gene of interest (GOI) by a commercial vendor

Clone GOI into *Tetrahymena* expression vectors



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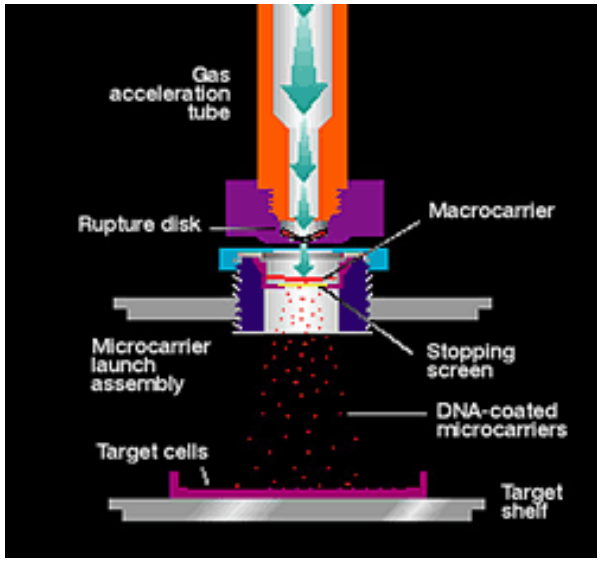
GENERALIZED WORK PLAN

Introduce expression vectors into Tetrahymena via biolistic transformation

↓

Selection of transformants in culture medium with antibiotic



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GENERAL WORK PLAN CONT.

Growth (up to 6L) of *Tetrahymena* culture

↓

Induction of gene expression using a heavy metal

↓

Breakup of cell culture using microfluidizer

Incubator for TTH growth

Shake flask

Microfluidizer

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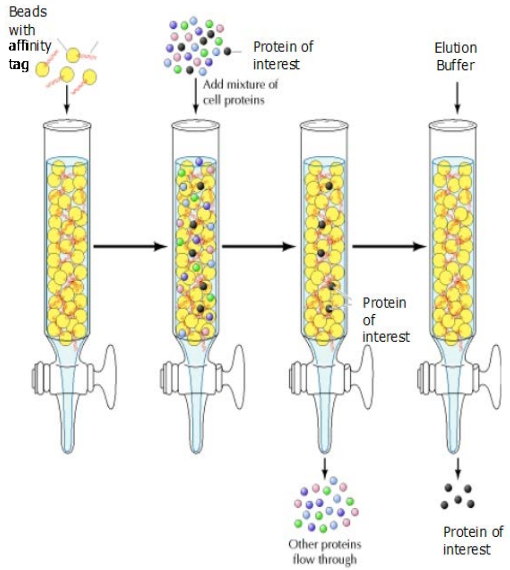
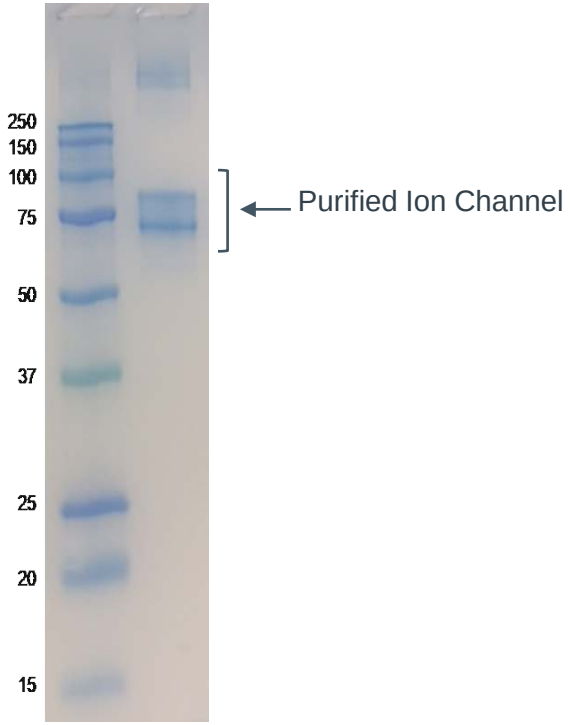
GENERAL WORK PLAN CONT.

- Recombinant proteins are extracted from Tetrahymena and purified using conventional chromatography techniques
- Purified proteins are then formulated for drug discovery campaigns



Traditional chromatography

Automated system – AKTA



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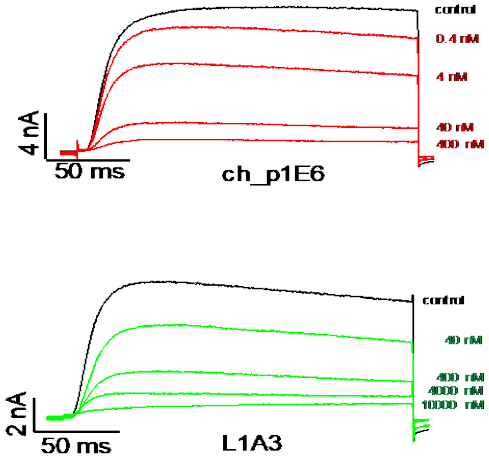
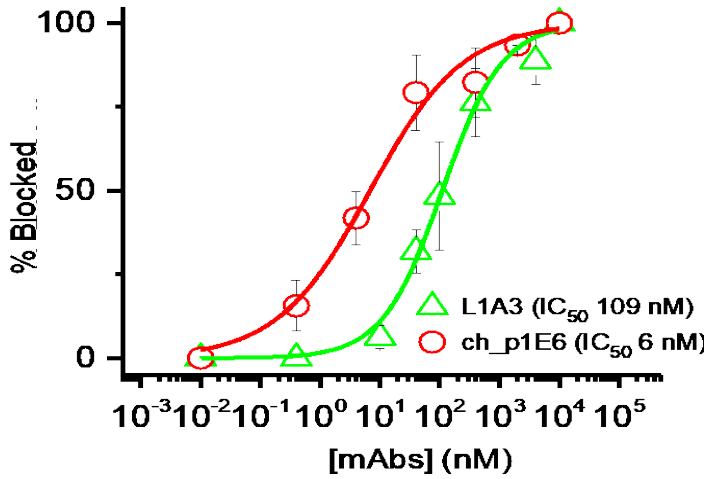
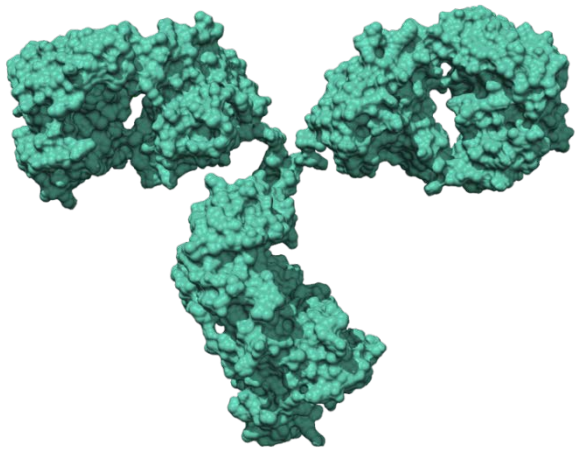
WORK DONE IN BL2 TISSUE CULTURE ROOM

- In-house characterization of drug candidates.
  - Drug candidates are screened and tested on mammalian cell strains (i.e. HEK293, CHO)
- These capabilities include:
  - FACS analysis
  - Specific mammalian cell assays
  - Electrophysiology
    - This is a technique specifically established to screen drug candidates that block ion channel function







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03 SAFETY SUMMARY

SAFETY OVERVIEW

- AbCellera Boston's rDNA activities in BL 1 lab:
  - Agents (e.g. *Tetrahymena thermophila, E. coli*) not associated with disease in healthy adult humans: Risk Group 1
  - All genes of interest are chemically synthesized and non-infectious
  - Minimal personal and environmental risk
- TetraGenetics' activities in BL 2 lab:
  - Agents that can cause human disease, but effective prophylaxis/treatment generally available; limited environmental risk
  - Work with established human cell lines is considered to be of low risk
  - CHO and HEK293 cell lines

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BIOSAFETY PROGRAM

AbCellera's Biosafety Manual and Exposure Control Plan updated in April, 2018 to include BL2 work. It describes:

Containment: Physical & Biological

✓ Lab design (easily cleaned/disinfected, sinks, insect/rodent control etc.) [BL1 and BL2]

✓ Lockable self-closing door, Biological Safety Cabinet [BL2]

Safe Work Practices

✓ Hand washing, no eating/drinking, decontaminating work surfaces etc. [BL1 and BL2]

✓ Universal precautions, labeling equipment/storage areas with the universal biohazard symbol [BL2]

Personal Protective Equipment

✓ Safety glasses, lab coats, gloves as appropriate for work [BL1]

✓ Safety glasses, lab coats, gloves at all times [BL2]

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SAFETY PROGRAM CONT.

AbCellera Boston Biosafety Manual (cont.)

- Training Requirements (presentations updated in April, 2018 for BL2 work)
  - ✓Initial and when changes to program/requirements [BL1]
  - ✓Initial and annual training [BL2]
- Medical Surveillance
  - ✓Contract with Mt. Auburn Occupational Health [BL1 and BL2]
  - ✓Hepatitis B Vaccination Program [BL2]
- Spill Response
  - ✓Procedures for cleaning small scale and large scale [BL1 and BL2]
- Waste
  - ✓Managed per the requirements of the MA Sanitary Code (105 CMR 480) [BL1 andBL2]

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WASTE MANGEMENT

Biological waste is managed and disposed of per the requirements of the MA Sanitary Code:

Solid biological waste and sharps waste is packaged and picked up for disposal by Veolia Environmental Services.

Sharps (needles, Pasteur pipettes, razor blades, glass slides etc.) are disposed of in a rigid puncture-proof sharps container.

Liquid cultures of *Tetrahymena* and other bacterial cultures are disinfected with a 1:10 dilution of bleach, followed by 30 minute contact time, prior to disposal.

Biological waste generated from the BL2 lab will be managed using current practices. Waste will be kept covered at all times.

** Bleach, a sodium hypochlorite solution, is an EPA-approved broad-spectrum disinfectant that is effective against viruses, bacteria, fungi, and mycobacterium.*

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SAFETY RELATED PERMITS

Permit	Agency	Permit Holder
rDNA	Arlington Board of Health	TetraGenetics Inc.
Wastewater	MWRA	TetraGenetics Inc.
Flammable	Arlington Fire Department	TetraGenetics Inc.
Haz. Waste	Mass DEP/EPA	TetraGenetics Inc.

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04 2023 RESEARCH & BIOSAFETY UPDATES

2023 UPDATES – RESEARCH AND BIOSAFETY

- Will be bringing in a WAVE-25 bioreactor
  - The lab will now be doing “large-scale” production according to Arlington BOH
  - WAVE-25 bioreactor will be used for increasing the amount of Tetrahymena growth to 25L at a time
  - Only requires oxygen tanks and compressed air
  - Will be adding CdCl2 into the bioreactor for induction of Tetrahymena cultures
  - Need IBC approval to submit to BOH in order to begin this work

- CryoEM Preparation
  - Will be bringing the ability to make in-house grids for negative staining
  - This will require the purchase of 1mg of Uranyl acetate
  - Will amend chemical hygiene plan with the help of Beth
  - The amount of Uranyl acetate we are requesting to have on site is exempt from radiation license
  - From Beth: “We have confirmed with the Radiation Control Officer from the Mass RCP that the stock material is considered generally licensed material and needs to be disposed as radioactive waste through an approved waste vendor. For diluted solutions, there is a provision for sink disposal in Table II (Effluent Concentrations) and Table III (Monthly Releases to Sewers) in 105 CMR 120.296 if within all other regulatory sewer limits (e.g. MWRA), although disposing of dilute solutions as radioactive waste is also an option”

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05 FINAL STEPS

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FINAL STEPS

- Project registration approval
  - ➢Discussion/questions on project 001-2011, Heterologous protein expression from *Tetrahymena thermophila*
  - ➢Vote to approve project registration

- Approval of waste handling practices
  - ➢ Required by the Massachusetts Sanitary Code

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THANK YOU

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Title
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Institutional Biosafety Committee
AbCellera Boston
91 Mystic Street
Arlington, MA 02474

IBC Protocol: 001-2011

Recombinant or Synthetic Nucleic Acid Molecules Project Registration Form

Protocol Number: 001-2011 (December 2022 update)

Title: Heterologous Protein Expression in *Tetrahymena thermophila*

Principal Investigator:	Janna Bednenko
Address:	91 Mystic Street, Arlington, MA
Phone:	(617) 840-5413
Fax:	N/A
Email:	jbednenko@tetragenetics.com

The signatures below represent the acceptance of responsibility for completeness of this project registration form, and compliance with all local, state and federal regulations and laws pertaining to the use of nucleic acid molecules covered under this protocol. Copies of this protocol must be provided to the individuals working under it and to other TetraGenetics staff as requested or required.

Principal Investigator's Signature: ____  ____ Date:__01/03/2023_
Janna Bednenko

Program Director's Signature: ___  ____. _Date: _01/03/2023
Paul Colussi

This protocol has been reviewed and accepted by the TetraGenetics Institutional Biosafety Committee (IBC). Please note that approval is not final until the principal investigator receives written confirmation of the approval.

2215 Yukon St.
Vancouver, BC
Canada, V5Y 0A1
T 1.604.559.9005
abcellera.com

IBC Chairman:__ _ _____Joanna Proctor_____ Date: 12/21/2022
Joanna Proctor

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A. Project Classification

Please review the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules and then check the appropriate level for this project registration in the chart below. Consult with BSO/Safety to confirm projects under III-E or III-F.

Check	Level	Approval/Review	Examples
	III-A	NIH Director, RAC, IBC	A drug resistant gene transferred into a (new) microorganism if acquisition of gene may compromise disease control.
	III-B	NIH/OBA, IBC	The cloning of toxin molecules with LD_{50} < 100 ng/kg of body weight or experiments NIH determines are equivalent to a previously approved protocol under III-A.
	III-C	RAC, IRB, IBC	Recombinant or Synthetic nucleic acid molecules (or DNA or rDNA derived from rDNA/SNA molecules) transferred into humans.
✓	III-D	IBC†	Experiments using recombinant DNA/synthetic nucleic acids from Risk Groups 2, 3, or 4 (see below): in host vector systems, in non-pathogenic systems, in whole animals, whole plants. Experiments involving >10 Liters of culture. Experiments with Influenza viruses.
	III-E	IBC§	Recombinant DNA/Synthetic Nucleic Acid molecules involving no more than 2/3 eukaryotic virus agents, whole plants, arthropods, or transgenic rodents. Expression in B strains of *E. coli*.
	III-F	Exempt	Recombinant or synthetic nucleic acid molecules used in a variety of experiments. e.g., SNA that can't replicate or generate NA that can replicate, not found in organisms or viruses, single monochromal or viral DNA sources, or host DNA transferred to the same host or related species.

† Approval required before initiation.

§ Notify IBC when project is initiated. IBC approval required.

AbCellera

2215 Yukon St.
Vancouver, BC
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abcellera.com

B. Project Goals

Please give a brief summary of project goals stated in non-technical terminology.

Tetrahymena thermophila is a common, non-pathogenic pond water ciliate. The first "animal-like" cell to be grown in pure culture, *Tetrahymena* has served as a key model for basic research in cellular biology and genetics since the 1950's. Its development, physiology, biochemistry, and ultrastructure have been well studied, and its use as a model has yielded numerous insights. TetraGenetics Inc. has developed *Tetrahymena* as a powerful, scalable protein expression system for the manufacture of a wide range of important mammalian proteins (including ion channels, growth factors, full-length antibodies and enzymes). Current work focuses on expression of human ion channel proteins, using TetraGenetics TetraExpress™ platform, as a drug discovery tool

C. Technical Description of Experiments

Provide a technical description of experiments. Include enough detail that referencing other documents or scientific papers is not necessary.

<u>*Tetrahymena* Protein Production</u>

Genes of Interest (GOI) are synthesized by a commercial vendor and sent to TetraGenetics as a component of a pUC19 vector. This construct is transformed into *E. coli* One Shot Top 10 cells (Invitrogen) and selected for using Ampicillin 100 μg/ml. Through traditional cloning protocols the GOI is moved into TetraGenetics proprietary rDNA expression vectors.

Expression vectors are transformed into *Tetrahymena thermophila* through biolistic transformation using the PSD-1000/He Particle Delivery System (BioRad). Successful transformants are selected by growth in the presence of antibiotic. Clones are screened for protein expression using an assay appropriate for the target protein (i.e. Western blotting). The most common method is by growing cells in small scale (2-10ml) in complex peptone based medium, inducing gene expression with low amounts of cadmium chloride (1-2 μg/ml) and harvesting 1.0 ml cell lysates. Proteins are resolved on SDS-PAGE (BioRad) and transferred to a nitrocellulose membrane for western blotting. Alternatively, other strains may be cultured in small scale as described above and assayed for target protein activity by various analytical methods.

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After clone selection is complete, culture growth is scaled up to 500-1000 ml (x6) in large culture flasks in shaking incubators. Once cells have reached an appropriate density protein production is induced with cadmium chloride. Cell pellets are harvested by centrifugation then frozen at -80˚C. The target protein of interest is then purified using standard lysis and chromatography methods.

Drug Discovery

Purified recombinant proteins (typically human ion channels) are formulated for antibody drug discovery platforms. Antibody discovery is not performed at AbCellera Boston but is carried out by our parent company, AbCellera Vancouver, or its subsidiaries. Following the isolation of candidate antibodies, AbCellera Boston may carry out characterization of these antibodies that includes determining specificity of binding to the human ion channel target as well as screening for functional activity of candidate antibodies. Functional activity here is defined as modulation of ion channel function (either enhancing or inhibiting) by the antibody. This is carried out by a method called electrophysiology whereby the electrical current in human cells (such as HEK293 or CHO cells) producing the ion channel target is measured in response to addition of antibody. Biological efficacy assays for functional antibodies are typically carried out using human or transformed mammalian cell lines.

C.1. What is the source of the nucleic acids?

Include gene names and organism of origin.

Chemically synthesized DNA from outside vendor.

C.2. What is the nature of the nucleic acid segment to be inserted?

Does the insert code for a toxin, what percentage of viral genome is eukaryotic, etc?

Variety of proteins (membrane proteins, antibodies, viral surface antigens, industrial enzymes, growth factors etc.). Currently, >90% of genes synthesized encode human ion channels.

C.3. What hosts and/or vectors will be used?

List all prokaryotic and eukaryotic hosts.

E.coli One Shot Top 10 cells (Invitrogen) – all are K12 E.coli derivatives

Stable 4 (New England BioLabs)

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E. coli SHuffle (New England Biolabs)

pUC19

pET21a

Tetrahymena thermophila (Cornell University *Tetrahymena* Stock Center)

Proprietary vectors based on the backbone of a ribosomal DNA vector pD5H8

Standard commercially available mammalian expression vectors (e.g. pcDNA3.1)

Human Cell Lines and Chinese Hamster Cell Lines (as follows): HEK293, CHO-K1, H1792, H358, U-87 MG, LN229, hTRPC3-HEK293, SK-OV-3, LNCaP, PC-3, Raji, THP1, H9, hKCa3.1-CHO-K1, HeLa, SHSY-5Y, MCF7, hNav1.8-HEK293, ND7/23, hKv1.3-CHO-K1, Jurkat, Tetanus toxoid specific B-LCL, Tetanus toxoid specific T-cells, MBP specific B-LCL, MBP specific T-cells, CD4+ T Cells, PBMCs, WT115, HEP2G

C.4. Will non-recombinant microorganisms be used?

Describe other potential sources of microorganisms, such as etiologic agents, blood, tissues, etc.

None.

C.5. What is the scale of work?

Bench scale <9.9 liters, or production scale >9.9 liters

Bench scale <9.9 liters - each shake flask only has 500ml -1liter of culture
Production scale of >9.9 liters – will be implementing WAVE25 and growing up to 25 liters at a time in 2023

C.6. Will animals be used under this project registration?

Any necessary animal work (e.g. immunizations for antibody generation; disease-specific animal models) is performed off site by a subcontractor. All animal work is approved by subcontractor IACUC.

If yes, specify:

Host: Rat autoimmune models (RA, MS etc), Llama, chicken, rodent for immunizations with purified protein.

Vectors: None

Inserted DNA: None

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What fraction of eukaryotic viral genome is contained in the recombinant molecule?: N/A

C.7. Will plants be used under this project registration?

No.

If yes, specify: N/A
Host

Vectors

Inserted DNA

What fraction of eukaryotic viral genome is contained in the recombinant molecule?

D. Occupational Health and Safety

Please check off the categories below that apply to this protocol. Discuss in detail below what procedures will be followed to assure proper protection of personnel.

D.1. Please state biosafety level work will be conducted at and include a justification for choosing this level. Final containment levels are the decision of the IBC.

This work will involve both BSL1 (e.g., non-pathogenic *Tetrahymena* thermophila, *E. coli*) and BSL2 (i.e., human cells) agents/material.

Lab employees shall operate at BL2 containment following universal precautions as required by the Bloodborne Pathogen (BBP) standard when handling human cell lines. Policies and procedures mandated by the BBP regulation are covered in the AbCellera Boston Exposure Control Plan. The Hepatitis B Vaccination (HBV) is offered to all lab employees with potential occupational exposure to Bloodborne Pathogens.

Biosafety and Bloodborne Pathogens training is provided by the Biosafety Officer or designee. The principal investigator is responsible for safety training and technique specific training for those employees working under his/her project.

All work included in this project registration will be conducted according to the policies and procedures outlined in the Biosafety Manual and Exposure Control Plan, including but not limited to general handling, equipment use and waste procedures.

PI INITIALS:____JB_____

D.2. Other safety considerations

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Check	Hazard Category
	Radioisotopes (may require changes to MA radiation materials license)
√	Chemical Hazards
	Controlled Substances
	Primary Human Tissue (requires BBP training)
	Other

D.3. Use as much space as necessary to fill in fields below.

Specific Hazard	Hazard Category	Precautions
Cadmium chloride	Chemical	Made from stock in the fume hood wearing full personal protective equipment per CHP guidance; small quantities used; media with cadmium chloride collected as hazardous waste.
Tetrodotoxin *(*TTX*)*	Chemical	Less than 1 mg present onsite. Made from stock in the fume hood wearing full personal protective equipment per CHP guidance; small quantities used; media with TTX collected as hazardous waste.
U*ranyl Acetate*	Chemical	1mg of Uranyl acetate will be present onsite. PP per CHP guidance, very small quantities used and collected as hazardous waste

E. Personnel

Provide below the names, titles and training each person working under this protocol has received. Include number of years working with rDNA and specific details of experience. Use as much space as is necessary. A copy of each individuals CV must also be on file.

Name	Training/Yrs. Experience	Title
Paul Colussi, PhD	31 years	Senior Vice President, Research
Janna Bednenko, PhD	31 years	Head of Protein Expression and Genetics
Ashot Papoyan, PhD	19 years	Consultant, Electrophysiology
Joanna Proctor	12 years	Project Manager
Ellen Gulezian	6 years	Research Associate II
Claudia Zafra	5 years	Research Associate II
Christina Crivello	5 years	Research Associate II
Sunyia Hussain, PhD	13 years	Lead, Protein Biochemistry

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Sarita Paudyal	4years	Research Associate
Anna Kimeu	3 years	Research Associate
Dainan Li	8 years	Research Scientist
Patrick Jiang	12 years	Research Scientist
Josefina Hernandez	8 years	Research Scientist
Alina Rivera	3 years	Laboratory Technician
Casey Fraher	1 year	Laboratory Technician
Kaci Gilbert	1 year	Research Technician
Katalina Ciorobea	1 year	Laboratory Assistant
Niranjan Varma	8 years	Research Scientist

F. Location of nucleic acid Use

Please list room numbers or names where work will take place.

Main Lab (BL1); BL2 Tissue Culture Room

G. Transfer of Materials

Will any of the materials be shipped between facilities? Please copy chart for each co-investigator.

Small quantities of materials may be shipped to collaborators for additional testing.

Name	**AbCellera Biologics**
Address	2215 Yukon St
	Vancouver, BC V5Y 0A1 Canada
Phone	+1 604-559-9005

Name	**AbCellera Australia**
Address	AbCellera Australia Pty Ltd. Building 12 41-45 Bourke Road Alexandria NSW 2015 Australia
Phone	0458 078 750

Town of Arlington
Department of Health and Human Services
Office of the Board of Health
27 Maple Street
Arlington, MA 02476

Tel: (781) 316-3170
Fax: (781) 316-3175

Application for Permit to Work with Recombinant DNA and Biological Agents

Annual Fee: $500.00

1. **Please provide the following information:**

   Name of Institution/Company: AbCellera Boston, Inc.

   Local Address: 91 Mystic Street, Arlington MA 02474 Phone: (617) 500-7471

   Corporate Address: AbCellera Biologics, 2215 Yukon Street Vancouver, British Columbia V5Y 0A1

   Website: www.abcellera.com OR www.tetragenetics.com

2. **Please provide the following information on the Chief Executive Officer:**

   Name: Carl Hansen, PhD. Email: carl.hansen@abcellera.com

   Address: 2215 Yukon Street Vancouver, British Columbia V5Y 0A1 Phone: 604.559.9005

3. **Please provide the following information on the Biosafety Officer:**

   Name: Joanna Proctor, MSc. Email: Joanna.Proctor@abcellera.com

   Address: 91 Mystic Street, Arlington, MA 02474 Phone: (617) 209-4887

4. **Please answer the following questions:**
   - This application is for Biosafety Containment Level (circle all the apply):

     BSL-1 (circled) BSL-2 (circled) BSL-3
   - Which organism(s) will be used at the facility? Please identify BSL for each organism.

     -**BSL-1:** *Tetrahymena* thermophila, *E*.coli

     -BSL-2 Human Cell Lines and Chinese Hamster Cell Lines (as follows): CHO-K1, Raji, hKCa3.1-CHO-K1, HeLa, ND7/23, hKv1.3-CHO-K1, Jurkat, Tetanus toxoid specific B-LCL, Tetanus toxoid specific T-cells, MBP specific B-LCL, MBP specific T-cells, CD4+ T Cells, HEK293, H1792, H358, U-87 MG, LN229, SK-OV-3, LNCaP, PC-3, SHSY-5Y, MCF7, hNav1.8-HEK293; THP1, H9, hTRPC3-HEK293, Expi-CHO S, PBMCs
   - What is the maximum cumulative volume of culture that will be present in the facility at a given time? (Note: Use of more than ten (10) liters is considered Large-scale use.)

     - *Tetrahymena* thermophila cultures that are grown in 1000ml or 500ml volumes using 6L or 2.8L shake flasks respectively

     -Will be increasing to large scale volumes (25L) in a WAVE25 bioreactor in 2023
   - What is the total square footage of biological laboratory or manufacturing space, plus waste storage space?

     -Current: 9,000 sq ft

5. **Please submit the following items with this application:**
   a. Non-refundable application fee (made payable to the Town of Arlington) of $500.00.
   b. A copy of the following documents ONLY if there have been changes to the document within the past year:
      i. Institution's Health & Safety Manual
      ii. Employee Training Program
      iii. A plot plan showing the location of all facilities on the site, and a detailed floor plan of the facility. The floor plan must be drawn to scale and indicate the rooms in which experiments will be conducted, as well as the waste storage area.
      iv. A roster and current bios of the members of the Institutional Biosafety Committee.
      v. A copy of the Institution's insurance policy in accordance with Section 5 (12) of the Regulations. The Town of Arlington must be named as an additional insured.

6. **Authorization:**

   I hereby agree to the following:
   - To abide by the Town of Arlington Biosafety and Recombinant DNA Regulations (effective April 11th, 2012).

- To comply with all applicable federal, state and municipal laws and/or regulations.
- To consent and grant access to the Board of Health, its agent(s) or designee(s) for the purpose of inspection of facilities and records.
- To complete and submit an annual report, as described in the Regulations, by April 30th each year.
- To pay promptly to the Town of Arlington any costs or charges associated with the Regulations
- To report immediately, in accordance with the Regulations and all other applicable guidelines, laws and regulations, to all appropriate authorities any significant problems, violations or rDNA related accidents or illnesses
- To indemnify, defend, protect, and hold harmless the Town of Arlington, its selectmen, officers, agents and employees from and against any and all claims, demands, losses, damages, liabilities, fines, charges, penalties, administrative and judicial proceedings and orders, judgments, remedial actions of any kind, all costs and cleanup actions of any kind, and all costs and expenses incurred in connection therewith, including reasonable attorney's fees and costs of defense (collectively, the "losses"), directly or proximately resulting from the institution's negligence with regard to any acts, omissions or conduct in any way related to any activity covered by the Regulations, pursuant to its permit, its application therefore, or resulting from the Institution's failure to comply with the terms of the permit, the Regulations or the National Institute of Health Guidelines for Research Involving rDNA Molecules.

I _____ of _____
(Chief Executive Officer or Chief Legal Officer) (Institution)

do hereby swear and affirm that all of the facts contained in this application and all attachments are true.

date _____ /s/ _____

Middlesex, ss.

Subscribed and sworn before me on _____ 20_____

by_____

_____
Notary Public

For Office Use Only

Application received on this day _____ by: _____
(BOH Staff)

Questions regarding this application can be directed to:

Padraig Martin
Lead Health Compliance Officer
781-316-3170
pmartin@town.arlington.ma.us

Town of Arlington
Department of Health and Human Services
Office of the Board of Health
27 Maple Street
Arlington, MA 02476
Tel: (781) 316-3170
Fax: (781) 316-3175

Biosafety and Recombinant DNA Regulations

SECTION 1: AUTHORITY

On April 11, 2012 the Arlington Board of Health, pursuant to the authority granted under Massachusetts General Laws (M.G.L.), Chapter 111, Section 31, voted to adopt the "**Biosafety and Recombinant DNA Regulations**" to protect the public health of the community.

SECTION 2: APPLICABILITY/ PURPOSE

These regulations shall apply to all research, production, and other associated activities involving rDNA materials or Biological Agents undertaken within the Town of Arlington, Massachusetts. All such activities shall be undertaken only in strict conformity with these regulations and with current National Institutes of Health (NIH) Guidelines (hereinafter referred to as the "Guidelines") as defined below herein § 3. Any institution engaged in research or production involving rDNA materials or Biological Agents shall also comply at all times with any other applicable federal and state regulations covering such work, including regulations promulgated by the Centers for Disease Control (CDC), Occupational Safety Health Administration (OSHA), Environmental Protection Agency (EPA) Massachusetts Department of Environmental Protection (MADEP) and Massachusetts Department of Public Health (MADPH).

These regulations are promulgated to ensure proper safe guards are in place for work with Biological Agents and recombinant DNA (rDNA) within the Town of Arlington. These regulations promote the safe and responsible conduct of science by institutions utilizing Biological Agents and rDNA materials, and promote competency and adequate training of laboratory staff in laboratory safety.

SECTION 3: DEFINITIONS

Biological agent: any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa), or infectious substance, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious substance, or anything capable of causing death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment. [from the CDC Select Agents and Toxins Final Rule. 42 CFR § 73.1 Definitions]

BMBL: Biosafety in Microbiological and Biomedical Laboratories. The key recommendations for working with biological materials in the United States (US) published jointly by the CDC and the NIH.

BSL: Biological safety level. There are four biosafety levels which consist of combinations of laboratory practices and techniques, safety equipment, and laboratory facility containment. Each combination is specifically appropriate for the operations performed the documented or suspected routes of transmission of the infectious agents, and the laboratory function or activity.

Biosafety Level One Laboratory (BSL-1): All facilities that meet or exceed the criteria for Biosafety Level 1 containment, according to descriptions in the BMBL; appropriate for agents that are not known to cause disease in normal, healthy humans.

Biosafety Level Two Laboratory (BSL-2): All facilities that meet or exceed the criteria for Biosafety Level 2 containment, according to descriptions in the BMBL; appropriate for handling moderate-risk agents that cause human disease of varying severity by ingestion or through percutaneous or mucous membrane exposure.

Biosafety Level Three Laboratory (BSL-3): All facilities that meet or exceed the criteria for Biosafety Level 3 containment, according to descriptions in the BMBL; appropriate for agents with a known potential for aerosol transmission, for agents that may cause serious and potentially lethal infections and that are indigenous or exotic in origin

Biosafety Level Four Laboratory (BSL-4): All facilities that meet or exceed the criteria for Biosafety Level 4 containment, according to descriptions in the BMBL; appropriate for exotic agents that pose a high individual risk of life-threatening disease by infectious aerosols and for which no treatment is available

CDC: Centers for Disease Control and Prevention

EPA: Environmental Protection Agency

Guidelines: The most recent version of the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules published in the Federal Register, and any further amendments, wherever published, which are adopted by NIH, or any successor agency thereto.

In the event that the NIH shall abolish or discontinue its Guidelines, those Guidelines in effect at the time of such discontinuance shall remain in effect within the Town of Arlington until further written notice from the Board of Health.

Institution: Any single individual, group of individuals, or organization, whether public or private.

Institutional Biosafety Committee: (IBC) a committee established by an institution in accordance with the Guidelines and the terms set forth in these regulations

Large-scale: The use of more than ten liters of rDNA and/or Biological Agent culture. This threshold shall be based on the cumulative volume of culture in all vessels throughout the institution's facility, not just a single vessel or experiment.

MADEP: Massachusetts Department of Environmental Protection

MADPH: Massachusetts Department of Public Health

OSHA: Occupational Safety and Health Administration

Recombinant DNA molecules (rDNA): in the context of the Guidelines, rDNA molecules are defined as either: (i) molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i) above.

Select Agent: Biological materials that have been restricted by the Department of Health and Human Services (DHHS) and the Animal and Plant Health Inspectional Services (APHIS) because of a perceived risk of bioterrorism through improper possession or use. Laboratories that wish to conduct research on these materials must follow strict guidelines that include registration of the entity, laboratory, and personnel with DHHS/APHIS prior to obtaining agents and starting research.

Risk Group: NIH classification of microbiological agents based on association with and resulting severity of disease

Risk Group 1: Agents that are not associated with disease in healthy adult humans

Risk Group 2: Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available

Risk Group 3: Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions may be available

Rick Group 4; Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available

Any other terms, not specifically defined herein, shall have the meaning as defined in the Guidelines. If the Guidelines do not define the term, it shall have the meaning as is commonly used.

SECTION 4: PERMIT REQUIREMENT

Any institution proposing to process or use Biological Agents or rDNA must obtain a permit from the Arlington Board of Health before engaging in any activity, including construction or renovation of facilities.

SECTION 5: TERMS AND CONDITIONS

1) All rDNA materials and Biological Agents classified as Risk Group 4 agents by the Guidelines, or any work with rDNA materials or a Biological Agent that requires BSL-4 containment based on a biological risk assessment shall be prohibited in the Town of Arlington.
2) Institutions applying for a permit must complete and submit the Plan Review Packet for the use of Biological Agents and/or rDNA within the Town of Arlington. The Director of Health and Human Services or his or her designee will review said application and make its recommendation to the Board of Health. A hearing with the Board of Health will be scheduled within sixty (60) days after the application is filed to take action on the application. The period within which final action shall be taken may be extended for a definite period by mutual consent of the Board of Health and applicant.
3) Each institution must designate an individual as the point of contact for the permit process. This person may be the biosafety officer or responsible official or may serve the institution in another capacity.
4) Institutions must comply with this regulation and the Guidelines at all times.
5) Institutions must allow inspections of both facilities and records, as related to these regulations, in response to emergencies and at other times deemed necessary by the Board of Health.
6) All areas in which rDNA or Biological Agents are utilized shall be free of rodent and insect infestation.
7) Institutions must adhere to a Health and Safety Manual, prepared by the institution, which contains all procedures relevant to the use of Biological Agents and rDNA at all levels of containment at use at the institution. The manual shall also contain a plan for waste disposal in compliance with all applicable federal, state, and local laws or regulations.
8) Institutions must establish and implement a training program of safeguards and procedures for both laboratory personnel using Biological Agents and/or rDNA and non-laboratory personnel who may come into contact with these materials.
9) Each institution shall establish an Institutional Biosafety Committee (IBC) which shall meet at least annually. The IBC shall be established in accordance with the Guidelines defined above, except that the required composition of each IBC shall include at least one representative from the Town of Arlington, approved by the Board of Health. The community member of the IBC shall have no financial interest in the institution or any other institution in competition therewith, and such representative shall be bound to the same provisions as to nondisclosure and nonuse of proprietary information as all other members of the IBC, except to the extent necessary to alleviate any public health hazard.
10) In accordance with the Guidelines, the IBC, acting on behalf of an institution, shall review all rDNA and Biological Agent use for compliance with the Guidelines and

approve those projects that conform to the Guidelines. A description of each protocol approved by the IBC, including all organisms and the containment to be used, and a statement certifying that the experiment conforms with the Guidelines shall be filed with the Board of Health.

11) All institutions shall provide an appropriate medical surveillance program as determined by their IBC and consistent with the Guidelines. Each institution shall submit a description of its medical surveillance program and documentation regarding its implementation as part of its annual report.
12) Each institution shall complete an annual report by April 30 of each year. Said reports must include a summary of the work performed over the past year and addressing any ongoing work and in addition the following:
    a. Current list of IBC members
    b. Copies of the previous year's IBC meeting minutes
    c. Summary of research and any changes in the past year
13) All information sent to the Board of Health shall have all proprietary information and trade secrets removed therefrom. The full text shall remain on file in the records of the institution for inspection at all reasonable times by any member of the IBC or The Board of Health or its designee(s). The Board of Health and its designee(s) shall maintain the confidentiality of all proprietary information and trade secrets released to them by reason of these regulations to the extent permitted by law. As used in these regulations, proprietary information and trade secrets shall be defined as set forth in under the laws of the commonwealth of Massachusetts.
14) Every applicant shall submit evidence of, and maintain at all times while conducting activities regulated hereunder, a policy or policies of insurance against liability arising out of activities regulated hereunder, for general liability insurance, and contractual liability insurance covering any indemnification required hereunder or by separate agreement, each in an amount of at least $1,000,000 for personal injury or death to any one person, and at least $5,000,000 for personal injury or death from any one incident, and at least $1,000,000 for property damage, and in addition, the institution shall have in full force and effect any other particular or special policy of insurance required by law and the Town of Arlington shall be named as an additional insured in all such policies.
15) Each institution engaging in, or intending to engage in, any activities regulated hereunder agrees to indemnify, defend, protect, and hold harmless the Town of Arlington, its selectmen, officers, agents and employees from and against any and all claims, demands, losses, damages, liabilities, fines, charges, penalties, administrative and judicial proceedings and orders, judgments, remedial actions of any kind, all costs and cleanup actions of any kind, and all costs and expenses incurred in connection therewith, including reasonable attorney's fees and costs of defense (collectively, the "losses"), directly or proximately resulting from the institution's negligence with regard to any acts, omissions or conduct in any way related to any activity regulated hereunder, pursuant to its permit, its application therefore, or resulting from the institution's failure to comply with the terms of the permit, the Regulation of the Guidelines.
16) Permits shall be issued and renewed on an annual basis. The fee for issuance and renewal of permits will be set by the Town Manager.

SECTION 6: LARGE SCALE USE

1) Any institution intending to use Biological Agents or rDNA on a large scale requires the expressed written approval of the Arlington Board of Health prior to conducting any such activity.
2) Any currently permitted institution shall request approval to conduct large scale activity from the Board of Health at least thirty (30) days prior to the initiation of any large scale-related activity, which may include, but not be limited to, construction or renovation of facilities. The Board of Health shall act and make a decision on the request within a thirty (30) day period from receipt of the request. Approval request should come in the form of proposed floor plan of the large scale room and IBC application documenting the proposed research and risk assessment by the Biosafety officer/IBC committee. A formal presentation to the Board of Health may be required to review the materials submitted prior to the Board of Health making a final decision to approve the project(s).
3) Institutions which are not currently permitted shall request approval to conduct large scale activity as part of their application for a Biological Agent or rDNA use permit.
4) During the review of the institution's request, the Board of Health may request additional information from the institution pertaining to the proposed large scale activity.

SECTION 7: EMERGENCY RESPONSE

1) The institution shall report immediately, and in no case more than twenty-four (24) hours, to the Board of Health and any other appropriate authorities any significant problems with or violations of the Guidelines or these regulations, any significant Biological Agent or rDNA- related accidents or illnesses, and any accidental release representing a significant hazard to employees or the public. The initial report shall be provided verbally to the Board of Health, with a written report documenting the initial report to follow within 24 hours. The institution shall provide a final written report to the Board of Health within 30 days of the initial report. The final written report shall include, but not be limited to, information detailing causes, outcomes, response measures, corrective actions and subsequent preventive measures related to the incident.
2) The institution shall provide a plot plan showing the location of all facilities, and a floor plan showing the internal layout of all facilities.
3) The institution shall submit a plan for orienting representatives of the Health, Police and Fire Departments to the facilities and the procedures to be utilized in the event of an emergency.

SECTION 8: ENFORCEMENT

Enforcement of this Regulation shall be the duty and responsibility of the Arlington Board of Health or its designee(s).

SECTION 9: PENALTIES

1) A violation of any condition or restriction of a permit or provision of these regulations shall subject the violator to a fine of three hundred ($300) dollars, or by a criminal complaint in a court of competent jurisdiction. Each day on which any violation exists shall be deemed to be a separate and distinct offense.

2) Once a permit has been issued it may be revoked, suspended, or modified, by the Board of Health, or not renewed upon a determination, after due notice and hearing, that the institution involved has materially failed to comply with these regulations or the permit requirements, and terms and conditions, including adherence to the Guidelines.

3) Notwithstanding the above, the Board of Health, upon determination that any violation constitutes an immediate or severe threat to the public health and safety, may order the necessary remedial actions up to and including the immediate closure of any premises or laboratory engaging in or contributing to such threat, without prior notice and hearing but with subsequent notice and hearing within reasonable time.

SECTION 10: EXCLUSIONS

The provisions of this Regulation are not intended to apply to clinical, non-research operations of doctors, dentists and veterinarians within the Town of Arlington when governed by other local, state and federal agencies and regulations.

SECTION 11: SEVERABILITY

The provisions of this section are severable; and if any of the provisions of these regulations shall be held unconstitutional or otherwise invalid by any court of competent jurisdiction, the decision of such court shall not affect or impair any of the remaining provisions.

Arlington Board of Health

Michael Fitzpatrick, DMD, Chair
Gregory Leonardos
Marie Walsh Condon, MD

Town of Arlington
Department of Health and Human Services
Office of the Board of Health
27 Maple Street
Arlington, MA 02476
Tel: (781) 316-3170
Fax: (781) 316-3175

MEMORANDUM

To: Board of Health
From: Padraig Martin, Lead Health Compliance Officer
Date: July 6, 2023
RE: Fenway Market Tobacco Compliance Violations

Rotem Aloni, Regional Tobacco Program Coordinator for the Metro South-West (MSW) Tobacco-Free Collaborative, conducted tobacco compliance checks on behalf of the department at several permitted retail tobacco establishments in town on June 7, 2023. Fenway Market sold a package of Newport Red cigarettes to an underage individual at approximately 12:37 PM. This violation represents the second violation within a 36-month period.

The above action is in violation of state law entitled "An Act to Modernize Tobacco Control", 105 CMR 665.00: Minimum standards for retail sale of tobacco and electronic nicotine delivery systems and of the Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products**.**

According to the Town's REGULATION RESTRICTING THE SALE OF TOBACCO PRODUCTS AND NICOTINE DELIVERY PRODUCTS,

> "The violator shall receive:
>
> a) In the case of a first violation, a fine of one thousand dollars ($1000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for seven (7) consecutive business days.
>
> **b) In the case of a second violation within 36 months of the date of the current violation, a fine of two thousand dollars ($2000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for fourteen (14) consecutive business days.**
>
> c) In the case of three or more violations within a 36 month period, a fine of five thousand dollars ($5000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for thirty (30) consecutive business days"

Enclosed please find the following item:

1. Copy of the correction order dated 6/8/2023
2. Copy of the correction order dated 6/30/2022

Town of Arlington
Department of Health and Human Services
Office of the Board of Health
27 Maple Street
Arlington, MA 02476

Tel: (781) 316-3170
Fax: (781) 316-3175

Correction Order

June 8, 2023

HAND DELIVERED
Fenway Market
Attn: Samir Shaikh
203 Broadway
Arlington, MA 02474

On Wednesday, June 7th, 2023, the Arlington Board of Health conducted a compliance check of several permitted retail tobacco vendors in town. Please be advised your establishment sold a package of Newport Reds cigarettes to an underage individual at approximately 12:37 PM. This sale is in violation of 105 CMR 665.00: Minimum standards for retail sale of tobacco and electronic nicotine delivery systems and of the Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products.

Fenway Market violated the state law entitled "An Act to Modernize Tobacco Control", 105 CMR 665.000, and Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products by:

☒ **Sale of tobacco product to a person under the Minimum Legal Sales Age;**
☐ Sale of a flavored nicotine delivery tobacco product [flavored combustible and other traditional tobacco products are prohibited on and after June 1, 2020];
☐ Offered for sale a flavored nicotine delivery product [see above];
☐ Failure of a non-age restricted establishment to maintain a record from the manufacturer indicating that an unflavored nicotine delivery product has a nicotine content of 35 milligrams per milliliter or less;
☐ Other, see the below additional violations, with any necessary additional pages attached:

You are hereby ordered to comply with An Act to Modernize Tobacco Control, 105 CMR 665.000, and Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products. In addition, the following fines and actions apply against Arlington Convenience for violations of 105 CMR 665.000 and Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products:

☐ First violation: a fine of one thousand dollars ($1000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for seven (7) consecutive business days;
☒ **Second violation within a 36-month period from the first violation: a fine of two thousand dollars ($2000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for fourteen (14) consecutive business days;**
☐ Third violation within a 36-month period from the first violation or additional violations during that time period: a fine of five thousand dollars ($5000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for thirty (30) consecutive business days.

You are hereby ordered to pay the amount of **$2,000.00** by check or money order made payable to the Town of Arlington within twenty-one (21) days of receipt of this order to the address below:

Arlington Board of Health
27 Maple Street
Arlington, MA 02476

You are hereby ordered to attend a Board of Health hearing. This hearing will be held to determine any further enforcement proceedings, including the possible suspension of your permit. The meeting will be conducted online via remote participation. All attendees must register in advance for the meeting. After you have register for the meeting, Zoom will send you the meeting link which you will use to access the meeting. **The link to register for the meeting will be provided once a date and time have been set for the hearing. Details to follow.**

Failure to comply with this order may result in additional penalties as permitted by law.

Signed by:

Name: _____ Date: 6/4/2023

Padraig Martin, REHS
Lead Health Compliance Officer
Town of Arlington
27 Maple Street
Arlington, MA 02476

Town of Arlington
Department of Health and Human Services
Office of the Board of Health
27 Maple Street
Arlington, MA 02476

Tel: (781) 316-3170
Fax: (781) 316-3175

Correction Order

June 30, 2022

HAND DELIVERED
Fenway Market
Attn: Samir Shaikh
203 Broadway
Arlington, MA 02474

On Sunday, June 26th, 2022, the Arlington Board of Health conducted a compliance check of several permitted retail tobacco vendors in town. Please be advised your establishment sold a package of Newport Reds cigarettes to an underage individual at approximately 11:06 AM. This sale is in violation of 105 CMR 665.00: Minimum standards for retail sale of tobacco and electronic nicotine delivery systems and of the Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products.

Fenway Market violated the state law entitled "An Act to Modernize Tobacco Control", 105 CMR 665.000, and Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products by:

☒ **Sale of tobacco product to a person under the Minimum Legal Sales Age;**
☐ Sale of a flavored nicotine delivery tobacco product [flavored combustible and other traditional tobacco products are prohibited on and after June 1, 2020];
☐ Offered for sale a flavored nicotine delivery product [see above];
☐ Failure of a non-age restricted establishment to maintain a record from the manufacturer indicating that an unflavored nicotine delivery product has a nicotine content of 35 milligrams per milliliter or less;
☐ Other, see the below additional violations, with any necessary additional pages attached:

You are hereby ordered to comply with An Act to Modernize Tobacco Control, 105 CMR 665.000, and Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products. In addition, the following fines and actions apply against Arlington Convenience for violations of 105 CMR 665.000 and Board of Health Regulation Restricting the Sale of Tobacco Products and Nicotine Delivery Products:

☒ **First violation: a fine of one thousand dollars ($1000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for seven (7) consecutive business days;**
☐ Second violation within a 36-month period from the first violation: a fine of two thousand dollars ($2000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for fourteen (14) consecutive business days;
☐ Third violation within a 36-month period from the first violation or additional violations during that time period: a fine of five thousand dollars ($5000.00) and the Tobacco and Nicotine Delivery Product Sales Permit shall be suspended for thirty (30) consecutive business days.

You are hereby ordered to pay the amount of **$1,000.00** by check or money order made payable to the Town of Arlington within twenty-one (21) days of receipt of this order to the address below:

Arlington Board of Health
27 Maple Street
Arlington, MA 02476

You are hereby ordered to attend a Board of Health hearing on **Wednesday, July 13, 2022 at 5:00 PM**. This hearing will be held to determine any further enforcement proceedings, including the possible suspension of your permit. The meeting will be conducted online via remote participation. All attendees must register in advance for the meeting. After you have register for the meeting, Zoom will send you the meeting link which you will use to access the meeting. To register for this meeting, please visit: https://town-arlington-ma-us.zoom.us/meeting/register/tZYufuCgqjwtHtCOMZGzYaKdnv71MuVgVqiq

Failure to comply with this order may result in additional penalties as permitted by law.

Signed by:

Name: _____ Date: 6/30/2022

Padraig Martin, REHS
Lead Health Compliance Officer
Town of Arlington
27 Maple Street
Arlington, MA 02476